A TEXT-BOOK

OF

PHARMACEUTICAL CHEMISTRY

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BY

ARTHUR OWEN BENTLEY, PH.C.
DIRECTOR OF THE DEPARTMENT OF PHARMACY, UNIVERSITY COLLEGE, NOTTINGHAM

AND

JOHN EDMUND DRIVER, M.Sc. (LOND.), A.I.C.
LECTURER IN CHEMISTRY, UNIVERSITY COLLEGE, NOTTINGHAM

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PREFACE

This book has been written, in response to many requests, to meet the needs of those studying for the Pharmaceutical Society's Diplomas and for Degrees in Pharmacy. It includes the whole of the theoretical and practical pharmaceutical chemistry and general organic chemistry necessary for the Chemist and Druggist Qualifying Examination, and provides a groundwork in pharmaceutical chemistry for those reading for higher examinations.

Throughout the book it has been assumed that the student has previously completed a course in general inorganic chemistry, including qualitative and volumetric analysis, of the standard of the Pharmaceutical Society's Preliminary Scientific Examination, or of Intermediate Examinations for Degrees in Pharmacy.

We wish to thank Professor F. S. Kipping, F.R.S., for kindly reading through the bulk of the manuscript and suggesting many valuable improvements, and also for permitting us to include in the Appendix a scheme for the identification of organic compounds which is in use at this College. We also wish to acknowledge the help received from several of our colleagues, particularly Dr. H. S. Holden, Dr. J. B. Firth, F.I.C., and Mr. F. S. Watson, M.Sc. The illustrations were prepared for us by Mr. F. H. Clarke.

We are indebted to the Editor of the *Pharmaceutical Journal* for permission to draw upon articles, written by one of us, which have appeared from time to time in the *Journal*.

Full use has been made of the information contained in current standard works, and, in a large number of cases, original papers have been consulted.

A. O. B.
J. E. D.

University College, Nottingham,
September, 1925.

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INTRODUCTION

PHARMACEUTICAL Chemistry may be defined as that branch of applied chemistry which treats of the chemical substances used in medicine, their preparation, properties, and identification, and the methods employed in determining their purity.

Part I. of this book is concerned almost exclusively with the inorganic substances of the British Pharmacopœia.[1] The non-metals and substances derived from them are in each case prefaced by a few introductory remarks designed to recall to the student the essential facts which he has or should have acquired during his studies in general chemistry. In the case of the metals, such remarks are confined to introductory paragraphs immediately preceding the compounds of each element. In Part II., which gives a systematic account of organic chemistry, particular emphasis has been laid upon substances included in the Pharmacopœia.

In both Parts, official substances are distinguished by the type employed in the headings. The more important are denoted by their Latin titles being printed in the centre of the page in heavy capitals, the English names, and synonyms if any, being placed below in ordinary type, thus :

SPIRITUS RECTIFICATUS

Alcohol (90 per cent). *Syn.* Rectified Spirit

Official substances of lesser importance are indicated by the use of small heavy type at the side of the page for their Latin titles, followed by the English names in italics, and synonyms, if any, in ordinary type, thus :

Chloral Formamidum. *Chloral Formamide.* *Syn.* Chloral-amide.

It is important to understand the difference between a chemical compound and an official substance of the same name. The official substance is a commercial product which is required to comply with certain standards of purity, and which may, in some cases, be directed to contain small quantities of other substances, added for some special reason. Thus, Acidum Hydriodicum Dilutum is a solution of hydriodic acid of a certain strength, containing a small

[1] For convenience, the organic salts of metals are dealt with in Part I.

amount of hypophosphorous acid; and Chloroformum contains, in addition to chloroform, a small proportion of ethyl alcohol.

In the body of the text, when it is desired to imply that a substance mentioned is of official standard, the official Latin or English name, with capital initial letters, has been employed; for example, Solution of Ammonia, Solution of Ferric Sulphate, Ammonii Carbonas.

It is intended that the reading of this book should be accompanied by a study of the corresponding portions of the Pharmacopœia.

Practical Work

The following remarks should be read carefully by the student before beginning the practical study of the subject.

Preparations.—Some official substances are prepared on the large scale by methods which cannot be conveniently reproduced in the laboratory, and in these cases the manufacturing processes have been described in brief and general terms. It is important, however, that the student should himself prepare as many official compounds as possible, and, where practicable, full laboratory details have been given. When parts are mentioned, it is to be understood that solids are by weight in grammes, and liquids by measure in mils.

A knowledge of the usual methods of preparation of chemical substances will often be found of great assistance in affording indications as to the source of common impurities.

Properties.—A substance which has been prepared, or which is given to the student to be examined for impurities, should always be compared as to its general appearance and physical properties with the description of the substance given under the heading of Properties. Any special chemical tests for identity which are mentioned should be applied.

Tests for Impurities.—Before testing a substance for impurities it is necessary to identify it, if its identity is unknown; or otherwise to ascertain whether it is, in the main, what it is represented to be. The substance may be identified by the ordinary methods of qualitative analysis; and, to assist the student in this, analytical tables sufficient for the purpose are included in the Appendix. During the course of the analysis, valuable indications may be obtained as to the nature of impurities present.

The tests given for impurities other than metals have been made, as far as possible, independent of one another, and may be applied to separate portions of the substance.

In the case of metallic impurities, however, it is essential that the metals of each analytical group be removed by the usual methods of group analysis before testing for metals of subsequent groups. Generally, a solution containing about two grammes of the substance should be prepared. Separate portions of this solution are tested for each metal in the order given, and when a metallic impurity is found it is

removed from the main solution, portions of the filtrate being then tested for metals of later groups, and so on.

It need hardly be emphasised that the reagents employed in testing for impurities must themselves be analytically pure. When any doubt exists, the student should conduct blank tests on the reagents. Throughout the text the term "water" should be understood to mean distilled water.

The tests for impurities have usually been selected as being such that the student can easily and conveniently carry out in the laboratory, and are not necessarily the most delicate tests that could be employed in analytical practice.

Arsenic and Lead Limits.—The student should have a general knowledge of the official lead and arsenic limit-tests as described in Chapter XII. He should be able to estimate the quantity of lead present in any of the official substances for which a limit is prescribed, and should carry out at least one estimation for arsenic—this last not so much with the idea of obtaining an accurate result, which requires considerable experience, but in order to become familiar with the details of the process.

It has not been thought necessary to include descriptions of the various electrolytic and other modifications of the quantitative Gutzeit test as commonly employed in analytical laboratories.

Quantitative Estimations.—It is not feasible for the student to perform every volumetric exercise described in this book, but it is important that the selection should be as varied and representative as possible. To assist in the arrangement of courses of volumetric analysis, a classified list of estimations is given at the end of the book. Chiefly for the benefit of those studying for the higher examinations, a number of the more important gravimetric determinations of the Pharmacopœia have been included.

The details of procedure and the quantities to be employed in quantitative estimations are such as would be normally employed in practice, and do not, as a rule, adhere rigidly to the text of the Pharmacopœia. In this connection we quote the following from the Preface to the Pharmacopœia, p. xiv.: "In quantitative testing, the specified amounts of solid or liquid substances are to be regarded as proportions indicating official standards of purity; they are not necessarily prescribed as the weights or volumes to be actually used in the operations. . . . In short, the details of procedure in these and other chemical operations are now left to the skill and judgment of pharmacists and of analysts who are assumed to be fully trained".

Volumes have been expressed in terms of the millilitre, which is the one-thousandth part of the International Litre. This system is employed in the Pharmacopœia, and is becoming generally adopted in scientific work. Throughout, the abbreviation "mil", which is recognised by the Board of Trade, has been used.

The sign ≡ is used, in statements derived from equations, as meaning "is (or are) equivalent to".

PART I

INORGANIC

CHAPTER I

OXIDES OF HYDROGEN

WATER, H_2O

(Mol. Wt. = 18)

At the present day, the ordinary drinking-water obtained from public sources of supply is remarkably pure; the pollution by sewage, etc., of the rivers and streams from which water for general purposes is obtained has become almost non-existent, while purification in the way of filtration and destruction of organic matter has reached a very high standard. Nevertheless, as most springs and rivers at some time during their course pass over or through calcareous or clayey soils, it follows that traces of calcium and magnesium salts are often found in the otherwise pure product. For ordinary purposes it is neither necessary nor desirable to remove these; but when the water is to be used for scientific purposes, or in the preparation of medicines, the traces of dissolved salts may produce untoward results by precipitation, producing a cloudy solution, with loss of strength, and causing a variation in different samples of solutions which should be of the same strength.

It is useless to remove these dissolved salts by any of the processes for " softening " waters, since the corresponding sodium salts are left in solution. The only method for the complete removal of such soluble substances from the water is distillation, and the British Pharmacopœia directs that distilled water should be used in every case, excepting only the preparation of " aromatic waters," where this is unnecessary, as these are themselves prepared by distillation.

AQUA DESTILLATA

Distilled Water

Preparation.—Distilled water is directed to be prepared by distillation from good natural potable water. In practice, the water is usually distilled from a copper still and condensed in a " worm " condenser of block tin. Unless the still is of the continuous type, and in constant use, the first tenth collected is rejected on account of its liability to contamination by volatile impurities, such as

ammonia, carbon dioxide, hydrogen sulphide, or sulphur dioxide, some or all of which may be present in ordinary water. For similar reasons the last tenth is not distilled, since it may contain volatile substances produced by the decomposition of traces of organic matter, or by the hydrolysis of certain of the dissolved salts, for example :

$$MgCl_2 + H_2O \longrightarrow MgO + 2HCl.$$

It is advisable that distilled water should be kept in stoppered bottles which have been previously rinsed with hot distilled water, as contamination by micro-organisms is in this way rendered less probable.

Tests for Impurities. *Sulphate.*—Acidify with hydrochloric acid and add barium chloride solution. There should be no turbidity.

Chloride.—Add silver nitrate to the water previously acidified with nitric acid, when no opalescence should be produced.

Nitrate.—The brown ring test described on p. 35 is not sufficiently delicate for detecting traces of nitrate in distilled water. The following test is generally employed. Mix 1 mil of the water with 3 mils of pure concentrated sulphuric acid and a few milligrammes of brucine. No red colour should be produced.

Limit of Dissolved Solids.—When 200 mils are evaporated to dryness *on a water-bath*, not more than 0·01 gramme of solid residue should remain. If a higher temperature than that of the water-bath be employed, ammonium salts and certain organic impurities may be volatilised and escape detection.

Limit of Ammonia.—As traces of ammonia are always present in the atmosphere, it is very difficult to keep distilled water entirely free from it. The Pharmacopœia recognises this difficulty, but prescribes a *limit* test in the form of Nessler's reaction.

For this purpose, two specially made white glass cylinders (Nessler glasses) are taken. In one is placed 50 mils of water known to be ammonia-free, together with 0·5 mil of a dilute solution of ammonium chloride (Nessler's, =0·00315 per cent NH_4Cl) : in the other Nessler glass is placed 50 mils of the water to be tested. To the contents of each glass are added 2 mils of Nessler's reagent ("Alkaline Solution of Potassio-Mercuric Iodide", see *B.P.*, Appendix II.), whereupon any brown coloration produced in the sample to be tested should not be more intense than that produced in the sample of known ammonia content at the end of five minutes, the glasses being placed on a white tile and viewed from above.

Nessler's test is an extremely delicate one commonly used in water analysis, especially where sewage contamination is suspected. The solution yields with ammonia or an ammonium salt a brown precipitate :

$$2HgI_2 + 4NH_3 = NHg_2I + 3NH_4I,$$

which, in exceedingly dilute solutions, gives a yellowish-brown tint to the liquid.

Lead, Copper, and Iron.—To 50 mils of the water, contained in a Nessler glass on a white tile, add one drop of sodium sulphide solution, when no coloration should be produced (due to the formation of the sulphides of these metals).

Limit of Organic Impurities.—Use is made of the fact that potassium permanganate is readily reduced by most organic matter. Add to 250 mils of the water to be tested 0·1 mil of N/10 permanganate and 3 mils of sulphuric acid, and set aside for three hours at 15·5°.

The next step depends upon the liberation of hydriodic acid from potassium iodide by the sulphuric acid, the hydriodic acid being oxidised by the permanganate with liberation of iodine:

$$H_2SO_4 + KI = KHSO_4 + HI,$$
$$2KMnO_4 + 3H_2SO_4 + 10HI = K_2SO_4 + 2MnSO_4 + 5I_2 + 8H_2O.$$

Consequently, if a crystal of potassium iodide be added to the mixture of water, acid, and permanganate solution, iodine will be liberated by the permanganate; if, however, organic matter be present in the water in such quantity that the whole of the permanganate is reduced thereby during the three hours during which the liquid is set aside, then no iodine will be liberated. The detection of the free iodine is facilitated by the addition of starch mucilage, which, in the presence of the least trace of iodine, produces an unmistakable blue colour.

Aqua Aurantii Floris. *Orange-flower Water.*—Orange-flower water of commerce is obtained as a by-product in the preparation of oil of orange-flowers (Oleum Neroli). The oil is obtained by the distillation in steam of the fresh flowers of the bitter orange tree, and is found floating on the surface of the water that collects in the receiver; the lower, aqueous layer is saturated with the oil and constitutes the water of commerce. It is diluted immediately before use with twice its volume of distilled water.

Orange-flower water is directed to yield no reactions for lead or copper, which may easily be detected by the addition of sodium sulphide solution, dark-coloured precipitates of the metallic sulphides being produced. These impurities may be present owing to the importation of the water in metal containers, and if alcohol has been (wrongly) added as preservative, sufficient acetic acid may be formed by oxidation to dissolve traces of the oxides and carbonates of the metals forming the material of the vessel. The U.S.P. directs that the water shall be neutral or only slightly acid.

Aqua Laurocerasi. *Cherry-Laurel Water.*—This water is prepared by distillation of fresh, crushed cherry-laurel leaves with water. The leaves contain in separate cells prulaurasin (a glucoside) and prunase (an enzyme); in the presence of the enzyme the glucoside is hydrolysed by the water, producing hydrocyanic acid, benzaldehyde, and glucose (p. 300):

$$C_{20}H_{27}NO_{11} + 2H_2O \rightarrow C_6H_5 . CHO + 2C_6H_{12}O_6 + HCN.$$

Prulaurasin. Benzaldehyde. Glucose. Hydrocyanic acid.

The water contains the volatile products, benzaldehyde and hydrocyanic acid, the strength of the latter being determined, and the preparation finally adjusted, by the addition of hydrocyanic acid or water, to contain 0·1 per cent by weight of HCN.

The details of the volumetric test are discussed under Acidum Hydrocyanicum Dilutum (p. 302).

HYDROGEN PEROXIDE, H_2O_2

(Mol. Wt. = 34)

An aqueous solution of this substance is included in the British Pharmacopœia under the name of Liquor Hydrogenii Peroxidi.

Preparation.—The solution may be prepared by the action of a dilute mineral acid on barium peroxide, $BaO_2,8H_2O$. The commonest acids used are phosphoric, hydrochloric, and sulphuric; but whichever is employed the treatment is similar, varying only in the method of freeing the product from impurities. The barium peroxide is made into a thin cream with water, and gradually added to the diluted acid, care being taken to leave the solution somewhat acid. In the case of sulphuric acid the following equation represents the reaction:

$$BaO_2 + H_2SO_4 = BaSO_4 + H_2O_2.$$

Most of the excess acid is then precipitated as barium sulphate by the cautious addition of barium hydroxide:

$$H_2SO_4 + Ba(OH)_2 = BaSO_4 + 2H_2O,$$

leaving a dilute aqueous solution of hydrogen peroxide, which may be filtered from the precipitated sulphate.

During these reactions the temperature of the solution must not be allowed to rise above 10° or considerable loss of strength occurs by decomposition with evolution of oxygen, hydrogen peroxide being a very unstable substance.

The student may prepare small quantities of the peroxide for experimental purposes by adding sodium peroxide to cold, very dilute hydrochloric acid, but should remember that the solution will also contain sodium chloride:

$$Na_2O_2 + 2HCl = 2NaCl + H_2O_2.$$

LIQUOR HYDROGENII PEROXIDI

Solution of Hydrogen Peroxide

Properties and Tests for Identity.—A colourless and odourless liquid. Taste slightly acid. Easily decomposed by heat into water and oxygen.

Add a few drops to a mixture of 10 mils of water, one drop of solution of potassium chromate, 10 drops of diluted sulphuric acid, and 2 mils of ether. The result is a deep blue layer between the ether and the aqueous liquid, the colour being communicated to the ether on shaking.

This is an extremely delicate and characteristic test, capable of showing the presence of hydrogen peroxide in solutions as dilute as 0·0015 per cent. It depends upon the liberation of chromic acid from the chromate by the sulphuric acid:

$$K_2CrO_4 + H_2SO_4 = K_2SO_4 + H_2CrO_4.$$

This, in presence of hydrogen peroxide, is believed to form perchromic acid, $HCrO_4$, which then combines with more peroxide to form the deep blue compound, the composition of which is uncertain. The blue compound quickly decomposes in aqueous solution with evolution of oxygen, but is soluble in ether, in which solution it is more stable.

Tests for Impurities. *Barium.*—No white precipitate of barium sulphate should be produced on addition of sulphuric acid.

Acidity (Limit of).—Not more than 2·5 mils of N/10 sodium hydroxide should be required to neutralise 25 mils of the solution, using methyl orange as indicator. The solution keeps better if left slightly acid, and the Pharmacopœia recognises this, but places a limit on the degree of acidity.

Total Solids (Limit of).—When 100 mils are evaporated to dryness on a water-bath, not more than 1·0 gramme of solid should remain.

Tests for Strength.—The official solution is commonly said to be of "10 volumes" strength; other strengths, 15, 20 volumes, etc., are found in commerce. These terms indicate the number of volumes of oxygen gas yielded by one volume of the solution when used; thus 1 mil of a "10 vols." solution should yield 10 mils of free oxygen under suitable conditions.

The Pharmacopœia nitrometer method employed for the determination of this strength is an excellent one; it is simple in manipulation, and very accurate with ordinary care. It has the added advantage of taking into account only the actual hydrogen peroxide content of the solution, thus rendering useless any attempt to give a false indication of strength by the addition of small quantities of such substances as oxalic acid. Such an addition would be taken into account as hydrogen peroxide were the solution tested by titration with potassium permanganate; this method is, however, appended below as being one with which the student should be familiar, but the limitations of which he should realise. Potassium permanganate used in conjunction with a nitrometer is also subject to this disadvantage to some extent, and the method is a clumsy one compared with that about to be described.

For the purposes of the official nitrometer test the apparatus (Fig. 1) is charged with brine (saturated sodium chloride solution), the level of the liquid being brought to the top of the measuring

tube, A, by opening the tap and raising the pressure tube, B, then closing the tap. 2 mils of the hydrogen peroxide solution are introduced into the cup, and the tap cautiously opened, care

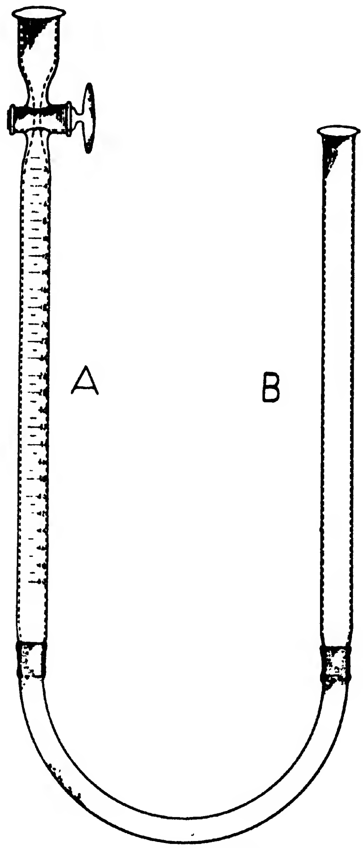


FIG. 1.—Nitrometer.

being taken to close it as the last drop enters the measuring tube in order that no air may enter. Any drops adhering to the side of the cup are rinsed into the tube with a little brine. 4 mils of copper ammonio-sulphate solution (*B.P.*, Appendix II.) are then admitted, taking the same precautions against the entrance of air.

As soon as the copper solution has entered the nitrometer, a brisk effervescence occurs, oxygen being evolved. The measuring tube is vigorously shaken to ensure the complete mixing of the reacting liquids, and, after an interval of about five minutes, the levels of the liquids in both tubes are brought to the same height by raising or lowering the pressure tube. The enclosed gas is then under atmospheric pressure, and its volume may be read. The Pharmacopœia states that this volume must be not less than 18 and not more than 22 mils at 15·5° and normal pressure, which, as 2 mils were used, corresponds to a strength of between 9 and 11 volumes.

The mechanism of this reaction is not very clear, but it may be assumed that the copper ammonio-sulphate solution acts as a solution of cuprous oxide, the oxide acting catalytically in that it combines with the available oxygen of the peroxide, but the compound produced is immediately decomposed, and the oxygen released.

The *percentage* of true hydrogen peroxide contained in a 10 volume solution may readily be calculated, as follows:

$$2H_2O_2 \longrightarrow 2H_2O + O_2.$$

68 grammes yield 32 grammes of oxygen
= 22·32 litres at N.T.P.[1]
= 22,320 mils ,,

22,320 mils O_2 are yielded by 68 grammes of H_2O_2 at N.T.P.[1]

11,160 ,, ,, 34 ,, ,, ,,

$$10 \quad ,, \quad ,, \quad \frac{34 \times 10}{11,160} \quad ,, \quad ,, \quad ,,$$

$$= \frac{34 \times 10 \times 273}{11,160 \times 288 \cdot 5} \text{ at } 15 \cdot 5° \text{ and N.P.}$$

$$= 0 \cdot 031 \text{ gramme.}$$

0·031 gramme is contained in 1 mil of the solution. 100 mils of the solution will contain 3·1 grammes = 3·1 per cent *w/v*, which for practical purposes in dispensing, etc., may be regarded as 3·0 per cent weight in volume.

The Potassium Permanganate Titration Method.—As mentioned above, the solution may be titrated with N/10 potassium permanganate if previously shown to contain nothing other than hydrogen peroxide which will affect this reagent.

Measure 5 mils of the peroxide solution with a burette, and dilute to 100 mils. Take 20 mils of the diluted solution, dilute, acidify with sulphuric acid, and titrate with N/10 permanganate until a permanent pink is just produced:

$$2KMnO_4 + 5H_2O_2 + 3H_2SO_4 = K_2SO_4 + 2MnSO_4 + 8H_2O + 5O_2.$$

Half the oxygen is yielded by the permanganate and half by the hydrogen peroxide, therefore,

[1] Because the molecular weight in grammes of any gas occupies 22·32 litres at normal temperature and pressure.

$2KMnO_4 \equiv 5O.$
$316 \equiv 80.$

316 grammes $KMnO_4 \equiv 5 \times 11 \cdot 16$ litres($=55,800$ mils) of oxygen
1000 mils of N/1 $KMnO_4 \equiv 5,580$ mils of oxygen.
1 mil of N/10 $KMnO_4 \equiv 0 \cdot 558$ mil of oxygen.

1 mil of the official solution should require between 16·2 and 19·9 mils of N/10 $KMnO_4$, corresponding to a strength of between 9 and 11 volumes, as permitted by the Pharmacopœia.

CHAPTER II

CHLORINE, BROMINE, AND IODINE

Of the halogen elements, fluorine, chlorine, bromine, and iodine, fluorine is of such little pharmaceutical interest as to require no mention here. The other three are important: chlorine and bromine on account of the extremely useful medicinal properties of their compounds; and iodine, not only on this account, but also owing to the frequent employment of the element itself in pharmacy.

CHLORINE, Cl_2

(Atomic Wt. = 35·5)

The element chlorine is a greenish-yellow gas with a pungent suffocating odour. It is extremely reactive, and unites with all the common metals to form chlorides, which will be discussed severally under the metals concerned.

Chlorine is not included in the Pharmacopœia as a medicinal substance, but is mentioned in Appendix I., *B.P.* (" Substances used in Chemical Testing "), where the usual laboratory method of preparation is given—*i.e.* by the interaction of manganese dioxide and hydrochloric acid:

$$MnO_2 + 4HCl = 2H_2O + MnCl_4,$$
$$MnCl_4 = MnCl_2 + Cl_2.$$

The resulting gas is passed through a little water contained in a gas-washing bottle. The wash-water retains the more soluble hydrochloric acid gas, should any come over, but soon becomes saturated with chlorine, allowing the remainder to pass on.

If the washed chlorine be now bubbled through distilled water until a saturated solution is obtained, we have Solution of Chlorine (Appendix II., *B.P.*, " Solutions employed in Chemical Testing ").

The solution of chlorine must be freshly prepared, for, on keeping, hydrochloric acid and oxygen are formed:

$$Cl_2 + H_2O = 2HCl + \hat{O}.$$

It is to the liberation of this nascent oxygen that chlorine, in the presence of water, owes its bleaching action.

A solution of chlorine is prepared frequently at the dispensing

counter by placing potassium chlorate in a dry bottle and adding to it concentrated hydrochloric acid. The bottle is lightly corked and allowed to stand for a short time (10 minutes), after which water is added a little at a time, shaking after each addition:

$$4KClO_3 + 12HCl = 4KCl + 6H_2O + 9Cl + 3ClO_2.$$

The solution will contain, in addition to chlorine, potassium chloride and some chlorine peroxide, which do not, however, interfere with its medicinal properties. The mixture of chlorine and chlorine peroxide obtained by this reaction was at one time believed to be a definite compound of chlorine and received the name *euchlorine*.

It is most important to note that when preparing such a solution of chlorine as that just described, the distilled water must be added from a measure, and not from the main supply, otherwise this will become contaminated by displaced gas. Suitable quantities for 100 mils of solution are 0·5 gramme of potassium chlorate and 1·8 mils of concentrated hydrochloric acid.

Chlorine is a powerful disinfectant, and is used principally for this purpose in the form of " bleaching powder " or chlorinated lime.

CHLORINATED LIME

This substance, often erroneously termed " chloride of lime ", and known commercially as bleaching powder, has the formula $Ca\langle^{OCl}_{Cl}$, and has been given the name calcium chloro-hypochlorite It may be regarded as a compound of calcium hypochlorite, $Ca(OCl)_2$, and calcium chloride, $CaCl_2$, in molecular proportions.

Preparation.—Bleaching powder is prepared on the large scale by acting upon calcium hydroxide with chlorine. The calcium hydroxide, which must be pure and fairly dry, is spread in a layer, several inches deep, on the asphalt floors of leaden chambers. A stream of chlorine is led into the chamber from the top, until the lime is saturated, the process being complete in from twelve to twenty-four hours:

$$Ca(OH)_2 + Cl_2 = Ca(OCl)Cl + H_2O.$$

Before opening the chamber, a stream of air is led through it in order to expel the excess of chlorine.

CALX CHLORINATA

Chlorinated Lime

Properties and Tests for Identity.—A dull white powder with a characteristic chlorinous odour, becoming moist and gradually decomposing with loss of chlorine on exposure to air. (For this reason it should be kept in air-tight containers in a cool, dry place.)

It is partially soluble in water, and in the presence of water splits up into calcium hypochlorite and calcium chloride:

$$2Ca(OCl)Cl \longrightarrow CaCl_2 + Ca(OCl)_2.$$

Test for calcium by shaking with water, filtering, and adding ammonium oxalate solution. A white precipitate of calcium oxalate is produced, soluble in dilute hydrochloric acid, but insoluble in acetic acid.

Test for chloride by shaking with water, filtering, acidifying the filtrate with nitric acid, and adding silver nitrate solution. A white precipitate of silver chloride is formed, soluble in ammonium hydroxide.

NOTE.—On the addition of acid, large quantities of chlorine will be evolved. (See below, *Quantitative Estimation.*)

Quantitative Estimation.—The Pharmacopœia requires that chlorinated lime shall yield not less than 30 per cent of available chlorine ("available chlorine" being the total amount of chlorine that can be liberated from it by the action of acids).

All the chlorine that the compound calcium chloro-hypochlorite contains may be released by the addition of an acid, according to the following equations:

$$Ca(OCl)Cl + 2HCl = CaCl_2 + HOCl + HCl,$$
$$HOCl + HCl = H_2O + Cl_2.$$

It will be seen that one molecule of chlorine may be obtained from one molecule of chlorinated lime; and if excess of potassium iodide be added to the solution in which this reaction is brought about, the liberated chlorine will displace an equivalent amount of iodine from this compound. The amount of iodine displaced may be estimated by titration with decinormal sodium thiosulphate solution, and from this the quantity of chlorine released can be calculated.

Weigh about 0·3 gramme of chlorinated lime in a stoppered weighing bottle, and rinse it into a titration flask containing about 1·2 grammes of potassium iodide dissolved in water; add a little diluted hydrochloric acid to this, and slowly titrate the solution with N/10 sodium thiosulphate solution until the brown colour is nearly discharged; then add a little more hydrochloric acid and more potassium iodide to ensure that these are present in sufficient quantity. Add a few drops of starch mucilage as indicator and continue to titrate until the blue colour is completely discharged.

If the bleaching powder be added to the water previous to the potassium iodide, or if the acid be added other than gradually, it is possible that some of the evolved chlorine may be lost:

$$Cl_2 + 2KI = 2KCl + I_2,$$
$$2Na_2S_2O_3 + I_2 = 2NaI + Na_2S_4O_6,$$
$$2Na_2S_2O_3,5H_2O \equiv I_2 \equiv Cl_2,$$
$$Na_2S_2O_3,5H_2O \equiv Cl,$$
$$248 \equiv 35{\cdot}5,$$

1000 mils N/1 $Na_2S_2O_3,5H_2O \equiv 35{\cdot}5$ grammes of chlorine,

1 mil N/10 $Na_2S_2O_3,5H_2O \equiv 0{\cdot}00355$ gramme of chlorine.

Liquor Calcis Chlorinatæ. *Solution of Chlorinated Lime.*—This is prepared by adding 10 per cent of chlorinated lime to water in a stoppered bottle, shaking occasionally during three hours, and filtering. It contains calcium hypochlorite and calcium chloride (see above, *Properties*), and is required to yield not less than 2 per cent of available chlorine.

Quantitative Estimation.—Measure 20 mils from a burette, and dilute to 100 mils in a stoppered flask. Using 20 mils of the solution for each titration, add potassium iodide solution and hydrochloric acid, and proceed as described under Calx Chlorinata.

Liquor Sodæ Chlorinatæ. *Solution of Chlorinated Soda.*—A paste of chlorinated lime is made by trituration with water, and to it is added a concentrated solution of sodium carbonate. The mixture is shaken occasionally during three or four hours, and the solution of sodium hypochlorite and sodium chloride thus produced is filtered from the insoluble calcium carbonate which is the other product of the reaction:

$$Ca(OCl)Cl + Na_2CO_3 = NaOCl + NaCl + CaCO_3.$$

Quantitative Estimation.—The solution is required to yield not less than 2·5 per cent of available chlorine when 5 mils are tested, as described under Calx Chlorinata:

$$NaOCl + NaCl + 2HCl = Cl_2 + 2NaCl + H_2O,$$

$$2Na_2S_2O_3,5H_2O \equiv I_2 \equiv Cl_2,$$

$$2 \times 248 = 2 \times 35{\cdot}5 \text{ grammes chlorine},$$

$$1000 \text{ mils } N/1\ Na_2S_2O_3,5H_2O = 35{\cdot}5 \quad \text{,,} \quad \text{,,}$$

$$1 \text{ mil } N/10 \quad \text{,,} \quad \equiv 0{\cdot}00355 \text{ gramme chlorine.}$$

BROMINE, Br_2

(Atomic Wt. = 80)

The element bromine is not official, and is little used in pharmacy. It is a dark red, volatile liquid with a choking odour, and occurs naturally in the form of magnesium bromide, which is found in the mother-liquor of the "salt mines" after the sulphates and chlorides have been removed by crystallisation. Manganese dioxide and hydrochloric acid are added to the mother-liquor, and the chlorine released displaces the bromine from its salts, the bromine being distilled off and condensed:

$$MgBr_2 + Cl_2 = MgCl_2 + Br_2.$$

Its compound with hydrogen, hydrobromic acid, HBr, and certain bromides are important medicinal substances which are considered later.

IODINE, I_2

(Atomic Wt. = 127)

Iodine is an element of great pharmaceutical importance, both the element and its compounds being largely used in medicine.

Preparation.—(1) Most seaweeds contain iodine, possibly the highest percentage (0·5 per cent) being contained in the dried stems of *Laminaria digitata*; *Fucus vesiculosus* contains much less. The dried seaweeds are burnt, and the ashes, or kelp, extracted with water. The solution is concentrated, potassium sulphate and potassium chloride crystallising out. The mother-liquor is treated with sulphuric acid, which decomposes the sulphides and thiosulphates with deposition of sulphur. The acid solution then contains only chlorides, bromides, and iodides, and is distilled with the proper amount of manganese dioxide, the liberated iodine being condensed in a series of earthenware condensers. The further addition of manganese dioxide results eventually in the liberation of bromine, when the condensers are changed. The iodine obtained in this manner is naturally liable to contain chlorine and bromine, from which it is freed by further distillation with potassium iodide, which forms the potassium salts of hydrochloric and hydrobromic acids with the liberation of an equivalent amount of iodine. This treatment also removes iodine chloride, ICl, and iodine cyanide, ICN, should either of these be present.

(2) The sodium nitrate beds which occur in Chili and Peru contain, in addition to this salt, small quantities of chlorides and iodates. The mineral—known as *caliche*—is treated with water, the mother-liquor remaining after crystallisation of the nitrate containing the dissolved iodates. On the addition of sulphurous acid, iodine is precipitated, according to the equation:

$$2KIO_3 + 5H_2SO_3 = K_2SO_4 + 4H_2SO_4 + H_2O + I_2.$$

The iodine is collected, dried over sulphuric acid, and sublimed.

(3) Small quantities may be prepared by heating sodium iodide, manganese dioxide, and sulphuric acid in a retort, the bluish-black crystals condensing in the neck of the retort and in the receiver:

$$2NaI + MnO_2 + 3H_2SO_4 = 2NaHSO_4 + MnSO_4 + 2H_2O + I_2.$$

IODUM

Iodine

Iodine of the Pharmacopœia is required to contain not less than 99 per cent of the element.

Properties and Tests for Identity.—It occurs in dark-coloured, rhombic prisms or octahedrons with a metallic lustre and character-

istic odour. Slightly soluble (1-500) in water, soluble 1-10 in alcohol (90 per cent). Readily soluble in a solution of potassium iodide (owing to the formation of a soluble salt, $I_2 . 2KI$) and in ether. All these solutions have a reddish-brown colour; but its solutions in chloroform, carbon disulphide, and liquid paraffin are violet in colour (the same colour as the vapour of iodine). It has been suggested, therefore, that in the case of a reddish-brown solution the iodine has combined with the solvent.

When gently heated, iodine yields a violet-coloured vapour. The melting-point of iodine is 113°, but it volatilises at ordinary temperatures as may be detected by its odour, and sublimes at temperatures below its melting-point. Below 700° iodine forms one of the heaviest vapours known, but at higher temperatures its density decreases, whence it is concluded that the molecule dissociates.

Iodine gives with mucilage of starch an intense blue colour which disappears on warming. A very characteristic reaction, capable of detecting even minute quantities.

Tests for Impurities. *Chlorine and Bromine.*—Shake 0·5 gramme with 20 mils of water and filter; to the filtrate add a slight excess of silver nitrate solution and shake. The precipitate will consist of silver iodide, together with traces of chloride, bromide, and cyanide, if these be present. Allow the precipitate to settle, pour off the supernatant liquid, and shake the residue with 10 mils of dilute ammonia (1 mil of Liquor Ammoniæ and 9 mils of water), when any chloride, bromide, or cyanide present will dissolve. Filter from the undissolved iodide and acidify the filtrate, when there should not be more than a slight opalescence (occasioned by re-precipitated silver cyanide, chloride, or bromide)

Iodine Cyanide.—If a little (0·1 gramme) iodine be heated in a small evaporating basin covered by a larger one filled with cold water, the first portion sublimed should not include any colourless prisms with a pungent odour. A more certain test consists in triturating 0·5 gramme with 20 mils of water and filtering. The filtrate will contain any iodine cyanide present and a little iodine. Decolorise by the careful addition of decinormal sodium thiosulphate solution; add potassium hydroxide, a little ferrous sulphate, and a drop of ferric chloride solution, warming gently. On the addition of excess of hydrochloric acid a blue colour develops if cyanide is present.

Moisture.—Dissolve in chloroform, when the solution should not possess the turbidity which water would produce if present.

Quantitative Estimation.—Weigh accurately about 1·0 gramme of iodine in a stoppered weighing bottle, dissolve in water containing about 3·0 grammes of potassium iodide, and adjust the volume to 100 mils. Take 20 mils of the solution for each titration, and run in N/10 sodium thiosulphate solution until the brown colour has almost disappeared; then add a few drops of starch mucilage and continue to titrate until the blue colour is discharged:

$$2Na_2S_2O_3 + I_2 = 2NaI + Na_2S_4O_6,$$
$$Na_2S_2O_3,5H_2O \equiv I,$$
$$248 \equiv 127,$$
$$1000 \text{ mils N/1 } Na_2S_2O_3,5H_2O \equiv 127 \text{ grammes iodine},$$
$$1 \text{ mil N/10 } Na_2S_2O_3,5H_2O \equiv 0{\cdot}0127 \text{ gramme iodine}.$$

Tinctura Iodi Fortis. *Strong Tincture of Iodine.*—Ten per cent *w/v* of iodine is dissolved in an aqueous solution of potassium iodide, and sufficient alcohol (90 per cent) added to produce the required volume. The amount of iodine present is estimated as just described, diluting 20 mils to 100 mils with water and taking 20 mils of the solution for each titration.

Tinctura Iodi Mitis. *Weak Tincture of Iodine.*—This is prepared similarly, but contains only 2·5 per cent of iodine. It may be estimated in the same manner.

Unguentum Iodi. *Iodine Ointment.*—Four per cent of iodine is dissolved in a solution of potassium iodide in glycerin, prepared lard added, and the mixture triturated until homogeneous. It may be assayed by the method of Evers and Elsdon. 5·0 grammes is dissolved in chloroform, 50 mils of water added, and the free iodine titrated with thiosulphate solution, with constant shaking. The free iodine is usually about 70 per cent of that actually added, as some combines with the unsaturated organic acids of the lard.

HYDROCHLORIC ACID, HCl

(Mol. Wt. = 36·5)

Muriatic Acid, Spirit of Salt

Preparation.—Hydrochloric acid is a colourless, fuming, readily soluble gas produced as a by-product in the first stage in the manufacture of sodium carbonate by the Le Blanc process (p. 70). In this process, crude sodium chloride and sulphuric acid are gently heated in large pans to produce sodium hydrogen sulphate and hydrogen chloride. The reaction is represented thus:

$$NaCl + H_2SO_4 = NaHSO_4 + HCl.$$

The gas is passed through earthenware pipes and is collected in water contained in earthenware receivers. The pasty residue of sodium hydrogen sulphate and sodium chloride is heated to redness in direct contact with the flame in a reverberatory furnace, when further quantities of hydrogen chloride are evolved:

$$NaCl + NaHSO_4 = Na_2SO_4 + HCl.$$

The acid produced by this second reaction is very impure, being contaminated by furnace gases.

Purification.—The hydrochloric acid produced by these reactions is the common, commercial "Spirit of Salt"; and is quite unsuitable for pharmaceutical purposes or for use as a reagent. The commercial acid may contain (i.) sulphuric acid, (ii.) ferric chloride, from the action of the acid on the iron of the apparatus, (iii.) sulphurous acid, from reduction of the sulphuric acid, (iv.) arsenic and selenium due to the use of impure sulphuric acid, and (v.) organic matter and foreign salts derived from the water used to dissolve the gas. These impurities may be removed by various methods, the simplest being the addition of, firstly, a small quantity of manganese dioxide, when the evolved chlorine oxidises the sulphurous acid to sulphuric acid and arsenious acid to arsenic acid, and, secondly, the addition of barium hypophosphite, when the whole of the sulphuric acid is precipitated as barium sulphate, the chlorine being converted into hydrochloric acid, and the arsenic precipitated as the element. The acid may now be decanted and distilled, the first tenth of the distillate, which is liable to contain traces of arsenic and chlorine, being rejected.

ACIDUM HYDROCHLORICUM

Hydrochloric Acid

The official acid is an aqueous solution of the gas required to contain 31·79 per cent by weight of HCl.

Properties and Tests for Identity.—A colourless and strongly acid liquid emitting white, pungent fumes. Specific gravity, 1·160.

Dilute and add silver nitrate solution, when a white precipitate of silver chloride is obtained, insoluble in nitric acid, but soluble in ammonium hydroxide.

Heat a little of the acid with manganese dioxide. Chlorine is evolved, and may be detected by its odour or by its imparting a blue colour to a piece of filter-paper which has been dipped into potassium iodide solution and starch mucilage.

Tests for Impurities (to be applied to the diluted acid). *Iron.*—Commercial hydrochloric acid invariably contains this, hence a slight reaction is permitted. Add nitric acid and potassium ferrocyanide, when only a very pale blue or green colour should be produced, not a deep blue.

Free Chlorine.—Dilute well, and add a solution of potassium iodide and starch mucilage, when no blue colour should be produced.

Sulphate.—There should be no precipitate on the addition of barium chloride solution.

Sulphite.—Add barium chloride, filter if necessary, and to the filtrate add bromine water, when any sulphite present is oxidised to sulphate and is precipitated as barium sulphate.

Iodide.—Add a little chlorine water and a few drops of carbon disulphide, when the carbon disulphide layer should not become

violet in colour, nor should the addition of starch mucilage produce a blue colour.

The precipitate with silver nitrate solution should be readily and completely soluble in ammonium hydroxide.

Bromide.—Add chlorine water and carbon disulphide, when the carbon disulphide layer should not become brown.

If iodide has been found the tests for bromide are not satisfactory until the iodide has been removed. To a portion of the diluted acid add sodium nitrite, and boil until all the iodine vapour has been expelled. Neutralise with sodium carbonate, evaporate just to dryness, dissolve the residue in a little cold dilute nitric acid, and add a crystal of potassium iodate. A brown colour, gradually developed, shows presence of bromide.

Dissolved Solids.—There should be no appreciable residue (less than 0·01 per cent) on evaporation.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—This is a simple titration with standard alkali for the amount of acid present. Weigh 10 grammes of the acid in a stoppered weighing bottle, and dilute to 100 mils in a graduated flask. Use 20 mils of the solution for each titration, employing methyl orange as indicator.

$$NaOH + HCl = NaCl + H_2O,$$
$$40 = 36{\cdot}5,$$
$$1000 \text{ mils } N/1 \ NaOH = 36{\cdot}5 \text{ grammes } HCl,$$
$$1 \text{ mil } N/1 \ NaOH = 0{\cdot}0365 \text{ gramme } HCl.$$

Acidum Hydrochloricum Dilutum. *Diluted Hydrochloric Acid.*—This is prepared by diluting 33 parts by weight of the concentrated acid to 100 parts by volume with water, the solution containing 10 per cent by weight of HCl. Specific gravity, 1·048. It should be free from the impurities mentioned under Acidum Hydrochloricum. The quantitative estimation is similar, using N/1 sodium hydroxide. Take 10 mils of the diluted acid for each titration.

HYDROBROMIC ACID, HBr

(Mol. Wt. = 81)

Preparation.—Hydrobromic acid cannot be prepared by acting upon a bromide with sulphuric acid, as some of it is oxidised by the sulphuric acid with liberation of bromine and sulphur dioxide; but it may be prepared in several other ways.

(1) The commonest laboratory method is to drop bromine from a dropping funnel upon red phosphorus, moistened with water, and contained in a retort. Phosphorus tribromide and pentabromide are first formed, and these are hydrolysed by the water with formation of phosphoric, phosphorous, and hydrobromic acids. The evolved

hydrogen bromide is collected in water until a solution of sufficient strength has been obtained:

$$PBr_3 + 3H_2O = H_3PO_3 + 3HBr,$$
$$PBr_5 + 4H_2O = H_3PO_4 + 5HBr.$$

(2) *Hydrobromic acid may be obtained from potassium bromide by the action of tartaric acid.* The two substances are dissolved separately and the solutions mixed; the mixture is cooled and allowed to stand for as long as possible, potassium hydrogen tartrate crystallising out:

$$KBr + H_2C_4H_4O_6 = HBr + KHC_4H_4O_6.$$

The acid obtained in this way is liable to contain potassium bromide, tartaric acid, and potassium hydrogen tartrate as impurity.

(3) When sulphur dioxide is passed into bromine water, the following reaction takes place:

$$SO_2 + 2H_2O + Br_2 = 2HBr + H_2SO_4.$$

The hydrobromic acid may be distilled off and collected in water. The product is very pure, but the process is not economical.

ACIDUM HYDROBROMICUM DILUTUM

Diluted Hydrobromic Acid

The official acid is required to contain 10 per cent by weight of HBr.

Properties and Tests for Identity.—A clear, colourless and inodorous liquid. Specific gravity, 1·077.

With silver nitrate solution a pale yellow precipitate is produced, soluble with difficulty in excess of ammonium hydroxide solution.

When heated with manganese dioxide bromine vapours are evolved.

Tests for Impurities. *Barium.*—No precipitate of barium sulphate should be produced on the addition of dilute sulphuric acid.

Sulphate and Sulphite.—Test as under Acidum Hydrochloricum.

Phosphate.—Neutralise with ammonium hydroxide, acidify with nitric acid, add excess of ammonium molybdate solution, and warm. No yellow precipitate should be produced.

Chloride.—Add excess of dilute nitric acid, and boil in a dish until bromine is no longer evolved. Transfer to a test tube, and add silver nitrate, when no white precipitate should be produced.

Dissolved Solids.—There should be no appreciable residue (less than 0·01 per cent) on evaporation.

Lead Limit.—5 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—In the case of hydrochloric acid the only volumetric test given in the Pharmacopœia is for acid present, because, since it is so cheap, sophistication with other acids is

unlikely; but, in the case of hydrobromic acid, this consideration does not apply, and in addition to the test for acidity, one is included for the actual amount of bromide present.

Test for Acidity.—Titrate with N/1 solution of sodium hydroxide, using 20 mils of the acid for each titration, methyl orange as indicator.

$$NaOH + HBr = NaBr + H_2O,$$
$$40 \equiv 81,$$
$$1000 \text{ mils N/1 } NaOH \equiv 81 \text{ grammes of HBr},$$
$$1 \text{ mil N/1 } NaOH \equiv 0{\cdot}081 \text{ gramme of HBr}.$$

Test for Quantity of Bromide.—Dilute 10 mils of the acid to 100 mils, and take 20 mils for each titration. Neutralise by the addition of a slight excess of calcium carbonate, and titrate with N/10 silver nitrate solution, a few drops of potassium chromate solution being used as indicator. The complete precipitation of all the bromide is shown by the appearance of a permanent red precipitate of silver chromate. If the acid is not neutralised prior to titrating, nitric acid will be one of the products, and this interferes seriously with the accuracy of the determination, owing to the action of the acid on the silver chromate.

$$CaCO_3 + 2HBr = CaBr_2 + CO_2 + H_2O,$$
$$CaBr_2 + 2AgNO_3 = Ca(NO_3)_2 + 2AgBr,$$
$$AgNO_3 \equiv HBr,$$
$$170 \equiv 81,$$
$$1000 \text{ mils N/1 } AgNO_3 \equiv 81 \text{ grammes of HBr},$$
$$1 \text{ mil N/10 } AgNO_3 \equiv 0{\cdot}0081 \text{ gramme of HBr}.$$

The amount of hydrobromic acid found by this method should correspond with that found by titration with alkali.

HYDRIODIC ACID, HI

(Mol. Wt. = 128)

Preparation.—The production of this compound from iodides by action of sulphuric acid is open to the same objection as mentioned under hydrobromic acid, large quantities of iodine being formed by oxidation of the hydriodic acid by the sulphuric acid.

(1) It can be prepared by an analogous process to that described for hydrobromic acid. 1 part of red phosphorus and 20 parts of iodine are introduced into a flask through the bung of which passes a wide delivery tube and a dropping funnel. Water is dropped very gradually from the funnel on to the mixture in the flask. When the reaction is complete, heat is applied and the evolved gas collected in water.

$$PI_3 + 3H_2O = 3HI + H_3PO_3,$$
$$PI_5 + 4H_2O = 5HI + H_3PO_4.$$

(2) Finely powder some iodine and suspend it in water. Pass

hydrogen sulphide gas into the liquid, when a little hydrogen iodide is formed. This brings about the solution of the remaining iodine by formation of a soluble, double salt, whereupon the reaction proceeds rapidly until a concentration of 48 per cent is reached, when action ceases.

$$H_2S + I_2 = 2HI + S.$$

The solution is then decanted or filtered from the precipitated sulphur.

(3) A solution of the acid may be obtained by the action of tartaric acid on potassium iodide.

ACIDUM HYDRIODICUM DILUTUM

Dilute Hydriodic Acid

The official solution is required to contain 10 per cent by weight of HI and 1 per cent by weight of hypophosphorous acid, H_3PO_2.

Properties and Tests for Identity.—A clear colourless liquid, which on keeping becomes brown owing to atmospheric oxidation with liberation of iodine.

$$4HI + O_2 = 2H_2O + 2I_2.$$

It is to counteract this that the Pharmacopœia requires the solution to contain 1 per cent of hypophosphorous acid, a very powerful reducing agent, which is gradually oxidised to phosphoric and phosphorous acids (see p. 81).

Add nitric acid and silver nitrate. A curdy yellow precipitate of silver iodide is formed, almost insoluble in ammonium hydroxide.

Add a few drops of chlorine water, and a little carbon disulphide. Iodine is liberated which dissolves in the carbon disulphide to produce a violet solution.

Test for the hypophosphorous acid in the solution by neutralising with ammonium hydroxide and adding a few drops of neutral ammonium molybdate solution, when a blue coloration or precipitate is produced, the colour being discharged on boiling.

Tests for Impurities. *Barium.*—No precipitate should be produced on adding ammonium sulphate.

Calcium.—There should be no precipitate on adding excess of ammonium hydroxide and ammonium oxalate solution.

Potassium.—(1) Evaporate to small bulk and apply the flame test (p. 51).

(2) To the concentrated liquid add a strong solution of sodium hydrogen tartrate. Set aside, scratching the side of the tube with a glass rod from time to time. No white crystalline precipitate of potassium hydrogen tartrate should be formed.

Sulphate.—Add hydrochloric acid and test with barium chloride. There should be no precipitate.

Sulphide.—Add hydrochloric acid and warm. A piece of lead

acetate paper held in the mouth of the tube should not be blackened.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—It is estimated by precipitation as silver iodide, and titration of the excess of silver nitrate with ammonium thiocyanate. Weigh about 25 grammes and dilute to 100 mils, using 20 mils for each titration. Add 45 mils of N/10 silver nitrate solution, 5 mils of strong nitric acid, and a few drops of ferric sulphate solution (made by boiling ferrous sulphate solution with a little nitric acid). The amount of silver nitrate that has not reacted with the hydriodic acid is then ascertained by titration with N/10 ammonium thiocyanate solution until a permanent pink colour is produced. This is not obtained until sufficient thiocyanate has been run in to react with the excess of silver nitrate, the next drop of the thiocyanate reacting with the ferric sulphate, which thus serves as indicator. By subtracting the number of mils of N/10 ammonium thiocyanate required from the number of mils (45) of N/10 silver nitrate originally added, the volume of the latter used to precipitate the hydriodic acid as silver iodide is found:

$$AgNO_3 + HI = AgI + HNO_3,$$
$$NH_4SCN + AgNO_3 = AgSCN + NH_4NO_3,$$
$$AgNO_3 \equiv HI,$$
$$170 \equiv 128,$$
$$1000 \text{ mils } N/1\ AgNO_3 \equiv 128 \text{ grammes of } HI,$$
$$1 \text{ mil } N/10\ AgNO_3 \equiv 0{\cdot}0128 \text{ gramme of } HI.$$

Syrupus Acidi Hydriodici. *Syrup of Hydriodic Acid.*—This is a 10 per cent *w/v* solution of diluted hydriodic acid in syrup and water. No tests are given in the Pharmacopœia.

CHAPTER III

SULPHUR AND ITS COMPOUNDS

SULPHUR, S

(Atomic Wt. = 32)

SULPHUR occurs in Nature, both free, and combined in the form of the sulphates of barium, calcium, and magnesium, and the sulphides of zinc, iron, copper, and mercury. In volcanic regions, notably Sicily and Italy, crude sulphur is found in the free state associated with native calcium sulphate and carbonate. It has been suggested that the deposits have been formed by the interaction of hydrogen sulphide and sulphur dioxide.

$$4H_2S + 2SO_2 = 4H_2O + 6S.$$

Another theory suggests that the deposits are due to the action of certain bacteria which are capable of absorbing the sulphur from hydrogen sulphide.

The crude sulphur is freed from earthy or siliceous matter by melting, the liquid sulphur being run off. It is next purified by sublimation, the vapours being passed into brick chambers. If the air in these is cool, the sulphur condenses in the air and falls in the form of a yellow powder, *flowers of sulphur*; if the air and walls of the condenser are sufficiently hot, however, the sulphur condenses as a liquid which may be collected in round wooden moulds to form the familiar *roll sulphur*, which consists of a mass of rhombic crystals.

Sulphur is also obtained from pyrites by slow burning, but there is considerable loss, and the product is liable to contain excessive quantities of arsenic.

Sulphur, heated near to its boiling point and poured into water, forms a soft mass of *plastic sulphur*, which, on keeping, reverts to the rhombic variety. Melted in air and allowed to cool until a crust forms on the surface, the liquid beneath, if poured out through one of two holes made in the crust, leaves amber-coloured needles of *prismatic sulphur*, which also reverts to the rhombic variety on keeping.

SULPHUR AND ITS COMPOUNDS

SULPHUR SUBLIMATUM

Sublimed Sulphur. *Syn.* Flowers of Sulph

Properties and Tests for Identity.—A slightly gritty, greenish yellow powder. Odourless and tasteless. Burns with a blue flam forming sulphur dioxide, SO_2, which may be recognised by it pungent odour, and the fact that it will blacken a strip of filte paper which has been dipped into mercurous nitrate solution.

Add a little to nitric acid and evaporate in a fume cupboard dissolve the residue in water, acidify with hydrochloric acid, and add barium chloride solution, when a white precipitate of barium sulphate is obtained, owing to the oxidation of the sulphur to sulphuric acid by the nitric acid.

Tests for Impurities. *Mineral Matter (Limit of).*—When ignited it should leave not more than 0·25 per cent of non-volatile residue.

Limit of Acidity.—During the heating of the sulphur prior to subliming it, traces of sulphuric anhydride are always formed. The Pharmacopœia recognises this, but fixes a limit as to the amount.

Shake 10 grammes with water, filter and wash the residue, when the combined filtrate and washings should not require more than 5 mils of N/10 sodium hydroxide solution for neutralisation, using phenolphthalein as indicator.

Unsublimed Powdered Sulphur.—Under the microscope sublimed sulphur should show, in addition to irregular angular particles, a due proportion of opaque globules. The absence of the latter would indicate the probability that powdered roll sulphur had been substituted for the sublimed product.

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—The Pharmacopœia does not give any test for strength, but the following is a summary of a method employed for this purpose:

A definite quantity of dried sulphur is boiled with a little 10 per cent potassium hydroxide solution until the liquid has a golden yellow colour. It is largely diluted, and a measured quantity acidified with hydrochloric acid, oxidised with excess of hydrogen peroxide solution, heated on a water-bath for half an hour, and then boiled. Excess of barium chloride solution is added, and the precipitated barium sulphate is washed, dried, and weighed, and the percentage of sulphur calculated from this.

Unguentum Sulphuris. *Sulphur Ointment.*—A mixture of 1 part of sublimed sulphur with 9 parts of benzoated lard.

Sublimed sulphur is employed here on account of the action of the angular particles in opening the burrows of the skin in which the acarids that cause the disease of scabies are found. The finer, precipitated sulphur would be useless for this purpose.

SULPHUR PRÆCIPITATUM

Precipitated Sulphur. *Syn.* Milk of Sulphur

Preparation.—When a solution of a thiosulphate is acidified with hydrochloric acid, sulphur dioxide is evolved and sulphur is precipitated in a fine form. This is due to the liberation of the very unstable thiosulphuric acid, which immediately decomposes into sulphur dioxide and sulphur.

$$Na_2S_2O_3 + 2HCl = 2NaCl + H_2S_2O_3,$$
$$H_2S_2O_3 = H_2O + SO_2 + S.$$

Sodium thiosulphate is too expensive to use for this purpose when large quantities are required. Precipitated sulphur is prepared in the laboratory by slaking 5 parts of lime, CaO, and mixing the product uniformly with 50 parts of water; to this 10 parts of sublimed sulphur are added, and a further 100 parts of water, the whole being boiled in a flask for one hour, with frequent agitation, when a complex mixture of thiosulphate, sulphide, and polysulphides of calcium is produced. The clear solution is decanted, the remainder filtered, and the clear liquids mixed. Hydrochloric acid is added in such quantity as to leave the liquid slightly alkaline, the precipitated sulphur being filtered off and washed on the filter until free from calcium, then dried at a moderate temperature. Some of the reactions which take place may be represented as follows:

$$3CaO + 6S = 2CaS_2 + CaS_2O_3,$$
$$2CaS_2 + CaS_2O_3 + 6HCl = 3CaCl_2 + 6S + 3H_2O.$$

Properties and Tests for Identity.—A greyish-yellow soft powder free from grittiness, burning with a blue flame when ignited, with formation of sulphur dioxide.

It may be oxidised to sulphate by nitric acid and tested as described under Sulphur Sublimatum.

Tests for Impurities. *Hydrogen Sulphide.*—It should be free from the odour of this gas, which may be produced by traces of calcium sulphide undergoing gradual decomposition due to the action of atmospheric moisture and carbon dioxide.

Sublimed Sulphur.—Only opaque globules should be visible under the microscope, without any angular or crystalline particles.

Mineral Residue (Limit of).—On ignition, not more than 0·5 per cent of residue should remain.

Limit of Acidity.—Mix 10 grammes with water, filter and wash; mix the filtrate and washings, when not more than 2 mils of N/10 sodium hydroxide should be required for neutralisation, using phenolphthalein as indicator. This corresponds to not more than 0·1 per cent of sulphuric acid.

Calcium.—Shake 0·5 gramme with water acidified with hydrochloric acid (to dissolve insoluble calcium salts, if any); filter, render the filtrate alkaline with ammonium hydroxide, and add

ammonium oxalate solution. There should not be more than a slight turbidity.

Chloride.—Shake about 1 gramme with water, filter, acidify the filtrate with nitric acid, and add silver nitrate solution. There should be no more than a slight opalescence.

Sulphate.—Treat about 1 gramme with water as before, acidify the filtrate with hydrochloric acid, and add barium chloride solution. There should not be more than a slight turbidity.

Alkalinity.—Shake about 2 grammes with water, and filter; the filtrate should not be alkaline to litmus paper.

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—No test for strength is included in the Pharmacopoeia, but the method summarised under Sublimed Sulphur may be employed if required.

Not Official

LAC SULPHURIS.—Milk of Sulphur.

This name is now used as a synonym for precipitated sulphur, but at one time it was applied to sulphur which had been precipitated from solution of a thiosulphate or polysulphide by *sulphuric acid*, a somewhat inferior product resulting.

SULPHUR LOTUM.—Washed Sulphur.

This is a form of sublimed sulphur which has been purified by washing with ammonia solution to remove all acid, and further washing on the filter to free from ammonia.

SULPHURIC ACID, H_2SO_4

(Mol. Wt. = 98)

Commercial Preparation.—Sulphuric acid is manufactured on a very large scale from pyrites, FeS_2, and there are two common processes, with the details of which the student will have become familiar during his studies in general Chemistry, so that only a brief summary of the more important facts will be given here.

(1) *The Leaden Chamber Process.*—Sulphur dioxide, obtained by the combustion of pyrites in air, is allowed to mix with nitrogen peroxide, the latter being formed by the decomposition of sodium nitrate in " nitre pots ". Sulphur dioxide, under ordinary circumstances, will not combine to any appreciable extent with atmospheric oxygen, but will combine with some of the oxygen of nitrogen peroxide. The mixed gases (sulphur dioxide, nitrogen peroxide, and air) are led into a series of chambers into which steam is blown, and the sulphur trioxide formed by oxidation of the dioxide combines with the water to produce a 60 to 70 per cent sulphuric acid, which collects at the bottom of the chambers:

$$NO_2 + SO_2 = SO_3 + NO,$$
$$SO_3 + H_2O = H_2SO_4.$$

The nitric oxide, NO, combines with the atmospheric oxygen to form nitrogen peroxide again, so that a small amount of nitrogen peroxide can bring about the oxidation of a relatively large quantity of sulphur dioxide.

The acid obtained from the chambers is concentrated by evaporation, first in lead-lined pans, and afterwards, as the acid becomes more concentrated, in silica pans.

Iron pyrites nearly always contains arsenic, and the commercial "oil of vitriol" generally contains this impurity, and also lead sulphate, oxides of nitrogen, mineral matter, and charred vegetable matter. The acid is purified by, first, diluting with from 10 to 20 times its volume of water, when any lead sulphate present is deposited, concentrating, and then distilling to free from dissolved mineral matter. The arsenic may be removed by the addition of a little barium sulphide to the crude acid before distillation, the arsenic being precipitated as sulphide and the barium as sulphate.

(2) *The Contact Process.*—Sulphur dioxide *will* combine with atmospheric oxygen in the presence of hot, finely divided platinum, and this fact is taken advantage of to prepare a very pure acid commercially. A mixture of cold, dry, carefully purified sulphur dioxide and air is led through tubes containing platinised asbestos on perforated plates. The tubes are contained in a chamber which is at first heated, but, as the reaction increases, the external heating is discontinued, and the asbestos prevented from becoming too hot by circulating the cold gases round the tubes before they come into contact with the catalyst.

The sulphur trioxide formed escapes as vapour and is collected in concentrated sulphuric acid, forming *disulphuric acid*, $H_2S_2O_7$, which may be diluted to produce the ordinary concentrated acid.

The efficient working of this process requires that the sulphur dioxide shall be in a state of extreme purity, or the catalytic action of the platinum soon ceases. For many years this was very detrimental to the commercial success of the process, but the difficulty appears to have been overcome, and year by year the output from this source increases, and it seems not unlikely that the leaden chamber process, the product from which requires so much purification, will eventually become obsolete.

ACIDUM SULPHURICUM

Sulphuric Acid

The official acid contains not less than 95 per cent by weight of H_2SO_4.

Properties and Tests for Identity.—A colourless, corrosive, intensely acid liquid of oily consistence, evolving much heat on the addition of water. Specific gravity, about 1·841.

To the diluted acid add barium chloride. A copious white

precipitate of barium sulphate is formed, insoluble in hydrochloric acid.

Add to the diluted acid, previously neutralised, lead acetate solution, then a little alcohol. A white precipitate of lead sulphate is obtained, soluble in ammonium acetate solution.

Tests for Impurities. *Copper.*—Dilute, add excess of ammonium hydroxide and filter. The filtrate should have no blue tinge, and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—Dilute, add nitric acid and potassium ferrocyanide. There should be no blue or green coloration.

Ammonium.—Dilute, add excess of sodium hydroxide, then boil. Test the evolved vapours with turmeric paper.

Chloride.—Dilute well and add silver nitrate, when there should be no precipitate or opalescence.

Nitrite.—Add to the *well-diluted* acid a crystal of ferrous sulphate. If nitrite be present the crystal will be turned brown.

Nitrate.—Pour a little of the concentrated acid carefully down the side of a tube containing cold ferrous sulphate solution, when no brown ring should be produced at the junction of the liquid.

If nitrite has been found, this must be destroyed before testing for nitrate. Boil the neutralised acid for a few minutes with a little ammonium chloride, when the nitrite is decomposed according to the equation

$$NaNO_2 + NH_4Cl = NaCl + 2H_2O + N_2.$$

Cool; add a small crystal of potassium iodide and a little starch mucilage, when, if the nitrite has all been destroyed, no blue colour will be produced. Add hydrochloric acid and a scrap of zinc to reduce the nitrate, if present, to nitrite. The appearance of a blue colour proves nitrate to have been present.

Sulphite.—To the diluted acid add excess of barium chloride, and filter. To the filtrate add bromine water, when any sulphite present will be oxidised to sulphate, and a further white precipitate of barium sulphate will appear (p. 30).

Selenium.—Dissolve a little sodium sulphite in hydrochloric acid and pour cautiously on to an equal volume of the suspected acid. A pink or red colour at the junction of the liquids indicates selenium.

Non-volatile Solids.—Add excess of ammonium hydroxide to a little of the diluted acid and evaporate, finally igniting, when there should be no appreciable residue (less than 0·05 per cent).

Lead Limit.—20 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—Weigh accurately about 5 grammes of the acid in a stoppered weighing bottle, and dilute to 100 mils. Take 20 mils for each estimation, titrating with N/1 sodium hydroxide solution, and using methyl orange as indicator:

$$2NaOH + H_2SO_4 = Na_2SO_4 + 2H_2O,$$
$$2NaOH \equiv H_2SO_4,$$
$$2 \times 40 \equiv 98,$$
$$1000 \text{ mils N/1 NaOH} \equiv 49 \text{ grammes of } H_2SO_4,$$
$$1 \text{ mil N/1 NaOH} \equiv 0{\cdot}049 \text{ gramme of } H_2SO_4.$$

Acidum Sulphuricum Dilutum. *Diluted Sulphuric Acid.*—This contains 10 per cent by weight of H_2SO_4, and is made by diluting the concentrated acid to a specific gravity of 1·069, or to such a strength that 10 mils require 21·7 mils of N/1 sodium hydroxide for neutralisation. The product should be free from the impurities mentioned under Acidum Sulphuricum.

The acid should be poured down a guiding rod a little at a time into the water, and not the water into the acid, or there will be a danger of spurting which may result in serious injury to the eyes. The development of heat which occurs is attributable to the chemical action which takes place, some of the water combining with the acid to form a hydrate.

Acidum Sulphuricum Aromaticum. *Aromatic Sulphuric Acid.*—This preparation, sometimes called " elixir of vitriol ", is prepared by adding sulphuric acid to alcohol gradually, then cooling to 15·5°, and adding spirit of cinnamon, tincture of ginger, and sufficient alcohol to produce the required volume.

Test for Strength.—The Pharmacopœia directs that the preparation shall be titrated with N/1 sodium hydroxide to determine the amount of sulphuric acid present, and this may be done in accordance with the directions given under Acidum Sulphuricum, diluting largely in order that the colour of the preparation shall not mask the colour change in the indicator.

When sulphuric acid is added to alcohol some ethyl hydrogen sulphate is formed in accordance with the equation

$$C_2H_5OH + H_2SO_4 = C_2H_5 . HSO_4 + H_2O.$$

The Pharmacopœia seems to presume that the ester will be immediately hydrolysed by the alkali, and that a simple titration will estimate the total quantity of acid that has been added ; but it must be remembered that ethyl hydrogen sulphate is not readily hydrolysed by alkali, and it has been shown (*Pharm. J.*, 1921, 2, 52, 136) that one week after it had been prepared, a sample of the acid no longer answered the official requirement as to acidity, and the less so the longer it was kept. It would seem better to estimate the amount of sulphuric acid, free and combined, by diluting, boiling with excess of standard sodium hydroxide, and back-titrating with standard acid.

SULPHUROUS ACID, H_2SO_3

(Mol. Wt. = 82)

Preparation.—Sulphurous acid is prepared by passing sulphur dioxide into water:

$$H_2O + SO_2 = H_2SO_3.$$

The sulphur dioxide may be easily obtained by the reduction of sulphuric acid with charcoal. Introduce into a 250-mils flask about 10 grammes of charcoal in coarse powder and 30 mils of sulphuric acid. Connect the flask by means of bent glass tubing with the inlet tube of a gas-washing bottle containing about 30 mils of water, and the outlet tube of the washing bottle with a large flask containing about 250 mils of water. The inlet tube of the collecting flask should dip about one inch below the surface of the water contained in it. A second tube passing through the rubber bung of the collecting flask should be connected to a third flask containing water, the end of the tube dipping about one inch below the surface. This last flask must also have an outlet tube to allow of the escape of carbon dioxide.

The collecting flask must now be surrounded by ice-cold water, and a gentle heat applied to the mixture of acid and charcoal until a steady flow of gas commences.

$$2H_2SO_4 + C = 2SO_2 + CO_2 + 2H_2O.$$

After a time the liquid in the collecting flask may be tested volumetrically, the whole measured, and then diluted to pharmacopœial strength.

The water in the last flask serves as a trap to prevent the escape of any excess of sulphur dioxide into the atmosphere. Care must be taken to see that the flask containing the acid and charcoal is disconnected instantly the flow of gas ceases, or water may be sucked back and the flask fractured.

Sulphur dioxide may also be prepared by heating concentrated sulphuric acid with sulphur, copper, or zinc:

$$2H_2SO_4 + S = 3SO_2 + 2H_2O,$$
$$2H_2SO_4 + Cu = CuSO_4 + SO_2 + 2H_2O,$$

or by burning sulphur in air:

$$S + O_2 = SO_2.$$

ACIDUM SULPHUROSUM

Sulphurous Acid

The official acid contains 6·4 per cent of H_2SO_3, corresponding to 5 per cent by weight of SO_2.

Properties and Tests for Identity.—A colourless liquid with a pungent odour. Specific gravity, 1·025.

To the neutralised acid add barium chloride ; a white precipitate soluble in hydrochloric acid is obtained.

Add to the neutralised acid silver nitrate solution. A white precipitate of silver sulphite is produced, soluble in hot dilute nitric acid, and in ammonium hydroxide.

Potassium permanganate solution is decolorised by the addition of excess of the acid.

Add to the neutralised acid barium chloride, and hydrochloric acid until the precipitate is redissolved. The addition of bromine water now produces a white precipitate, owing to the oxidation of the sulphite to sulphate:

$$H_2SO_3 + Br_2 + H_2O = H_2SO_4 + 2HBr.$$

Tests for Impurities. *Sulphate* (*Limit of*).—The acid should not yield more than a slight precipitate with barium chloride.

Non-volatile Matter.—There should be no appreciable residue on evaporation (*in a fume cupboard*).

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—It is estimated by oxidation with standard iodine solution. Weigh about 5 grammes of the acid, dilute to 100 mils, and take 20 mils for each estimation. Dilute well with recently boiled and cooled water, and add 30 mils of N/10 solution of iodine. Then titrate with N/10 sodium thiosulphate solution to determine the amount of iodine that has not reacted with the sulphurous acid, starch mucilage being used as indicator. The number of mils of N/10 thiosulphate required, subtracted from the number of mils of N/10 iodine added at first will give the number of mils of iodine used:

$$H_2SO_3 + I_2 + H_2O = H_2SO_4 + 2HI,$$

$$I_2 \equiv SO_2 \equiv H_2SO_3,$$

$$2 \times 127 \equiv 64 \equiv 82,$$

$$1000 \text{ mils N/1 } I_2 \equiv 32 \equiv 41 \text{ grammes of } H_2SO_3,$$

$$1 \text{ mil N/10 } I_2 \equiv 0{\cdot}0032 \equiv 0{\cdot}0041 \text{ gramme of } H_2SO_3.$$

Carbon Disulphide, CS_2

(Mol. Wt. = 76)

Preparation.—This substance is obtained by heating charcoal and sulphur together at a moderate red heat, the product distilling and being collected in a series of condensers so arranged that any hydrogen sulphide formed may escape. Carbon disulphide usually has a very disagreeable odour owing to impurity, but after purification by repeated distillation over white wax and agitation with mercury it is nearly odourless.

CARBON DISULPHIDUM

Carbon Disulphide. *Syn.* Carbon Bisulphide

Properties and Tests for Identity.—A clear, colourless, highly refractive liquid with a characteristic but not fetid odour. It boils between 46° and 47°, and burns with a bluish flame, forming carbon dioxide and sulphur dioxide. Taste, sharp and aromatic. Specific gravity, 1·268. *Its vapour, mixed with air, is explosive.*

Tests for Impurities. *Free Sulphur.*—Allowed to evaporate spontaneously in an open glass vessel, it should leave no residue.

Hydrogen Sulphide.—It should not blacken lead acetate paper when agitated with it.

Sulphur Dioxide.—Moistened blue litmus paper should not be reddened by carbon disulphide.

CHAPTER IV

COMPOUNDS OF NITROGEN AND PHOSPHORUS

AMMONIA, NH_3

(Mol. Wt. = 17)

Preparation.—(1) Ammonia is prepared commercially by washing with water the gases obtained during the destructive distillation of coal in the production of coal gas. The " ammoniacal liquor " so produced is boiled with milk of lime to expel the gas, which, after passing through tubes containing charcoal, to free it from tarry matter, is collected in water to form the strong ammonia solution of commerce (see also p. 90).

(2) Ammonia may be prepared in the laboratory by heating an ammonium salt with alkali; for example:

$$2NH_4Cl + Ca(OH)_2 = 2NH_3 + CaCl_2 + 2H_2O.$$

LIQUOR AMMONIÆ FORTIS

Strong Solution of Ammonia

This is an aqueous solution containing 32·5 per cent by weight of NH_3.

Properties and Tests for Identity.—A colourless liquid, with a characteristic odour, evolving pungent fumes. Specific gravity, 0·888 (whence the common trade term for the solution—" eight-eighty ammonia "). A solution having this specific gravity contains nearly 800 times its own volume of the gas.

The solution is strongly alkaline. A piece of red litmus paper held near the mouth of the bottle becomes blue instantly; a piece of turmeric paper treated similarly becomes brown, changing to yellow on moistening with acids. On bringing a glass rod moistened with hydrochloric acid near the liquid, white fumes of ammonium chloride are produced.

Tests for Impurities. *Dissolved Solids.*—It should leave no appreciable residue on evaporation (in a fume-cupboard).

Tarry Matter.—Dilute with an equal volume of water, and *cautiously* add a slight excess of sulphuric acid. No yellow colour and no tarry odour should be noticeable. Next, evaporate some of

this liquid to dryness on a water-bath, when the residue should be colourless. On ignition the residue should be completely volatile.

Before applying the remaining tests the liquor may be boiled in a fume-cupboard to drive off some of the ammonia.

Copper, Iron, and Lead.—No colour, due to the sulphides of these metals, should be produced on the addition of 0·5 mil of sodium sulphide solution to 50 mils of the suspected liquor contained in a Nessler glass on a white tile.

Aluminium.[1]—Nearly neutralise with hydrochloric acid, and boil. A white gelatinous precipitate will be produced if aluminium be present. (Aluminium hydroxide is slightly soluble in excess of ammonia, but insoluble in presence of ammonium chloride.)

Zinc.—No white precipitate should be produced in the sodium sulphide test for heavy metals.

Calcium.—Ammonium oxalate solution should yield no white precipitate.

Magnesium.—Add sodium phosphate solution, shake well, scratch the sides of the tube with a glass rod and set aside. No white precipitate should be produced.

Sodium and Potassium.—Evaporate about 20 mils to dryness in the fume-cupboard and apply the flame test (p. 51) to the residue, if any.

Chloride.—Not more than a slight opalescence should be produced on adding excess of nitric acid, followed by silver nitrate solution.

Carbonate.—No white precipitate should be produced on the addition of lime water.

Sulphide.—Lead acetate solution should yield no *black* precipitate.

Sulphate.—Add excess of hydrochloric acid, then barium chloride solution. No precipitate should be formed.

Arsenic, Limit.—0·5 part per million (p. 176).

Quantitative Estimation.—It is estimated by neutralisation with standard acid. Weigh about 5 grammes in a well-stoppered weighing bottle, and dilute to 100 mils in a stoppered measuring flask. To 20 mils (measured from a burette) add 30 mils of N/1 sulphuric acid, then determine the amount of acid which has not combined with the ammonia by titrating with N/1 sodium hydroxide solution, using methyl orange as indicator. The volume of hydroxide required, subtracted from the volume of normal acid added, will give the number of mils of acid required by the ammonia, since equal volumes of normal solutions are equivalent:

$$H_2SO_4 + 2NH_3 = (NH_4)_2SO_4,$$
$$98 \equiv 2 \times 17,$$
$$49 \equiv 17,$$
$$1000 \text{ mils N/1 } H_2SO_4 \equiv 17 \text{ grammes of } NH_3,$$
$$1 \text{ mil N/1 } H_2SO_4 \equiv 0{\cdot}017 \text{ gramme of } NH_3.$$

[1] The test for aluminium should be applied to a portion from which the ammonia has not been expelled.

Liquor Ammoniæ. *Solution of Ammonia.*—This is an aqueous solution containing 10 per cent by weight of ammonia, NH_3, and may be prepared by diluting 1 volume of the strong solution with 2 volumes of water. Specific gravity, 0·959. In other respects the solution corresponds to the tests given under Liquor Ammoniæ Fortis.

Quantitative Estimation.—The method described for the strong solution is employed, using about 10 grammes, and diluting as before.

NITRIC ACID, HNO_3

(Mol. Wt. = 63)

Preparation.—(1) Nitric acid is prepared commercially by distilling sodium nitrate (Chili saltpetre) with sulphuric acid:

$$NaNO_3 + H_2SO_4 = NaHSO_4 + HNO_3,$$

and when the temperature is raised:

$$NaNO_3 + NaHSO_4 = Na_2SO_4 + HNO_3.$$

The retorts are usually lined with fireclay, and built into the furnace to ensure uniform heating. The last of the series of condensers is connected with a tower down which a stream of water descends, to absorb any nitrogen peroxide which might otherwise escape.

The acid in the condensers is reddish in colour, due to nitrogen peroxide, and contains a considerable amount of water. It is purified by redistillation with an equal volume of sulphuric acid (to free it from water), a stream of air being blown through the product to free it from nitrogen peroxide. The acid thus obtained may be of 99·6 per cent purity, when it has a specific gravity of 1·52. The commercial acid as supplied for ordinary use is never as strong as this, having a specific gravity of about 1·35 to 1·4, *i.e.* rather less than the official acid.

(2) Nitric acid may be prepared easily in the laboratory by distilling together equal weights of potassium nitrate and concentrated sulphuric acid in a glass retort, the distillate being received in a well-cooled flask.

ACIDUM NITRICUM

Nitric Acid

This is required to contain 70 per cent by weight of HNO_3 and 30 per cent by weight of water.

Properties and Tests for Identity.—A clear, colourless, very corrosive liquid, evolving choking fumes. Specific gravity, 1·42.

Warm a little in a test-tube with a fragment of copper. Reddish-brown fumes of nitrogen peroxide are evolved:

$$8HNO_3 + 3Cu = 3Cu(NO_3)_2 + 2NO + 4H_2O,$$
$$2NO + O_2 = 2NO_2,$$

the nitric oxide first produced combining with atmospheric oxygen.

To a little nitric acid in an evaporating basin, add a few drops of 1-400 solution of brucine in concentrated sulphuric acid. A gradually deepening red colour is produced, later changing to yellow. This is an extremely delicate test for nitric acid (or for metallic nitrates, if first treated with concentrated sulphuric acid), but it is not so useful in presence of bromides or iodides.

Dilute, add a cold solution of ferrous sulphate, then pour some concentrated sulphuric acid down the sides of the tube in such a manner that it forms a layer at the bottom. A brown ring forms at the junction of the liquids, due to the liberation of nitric oxide from the nitrate:

$$2HNO_3 + 3H_2SO_4 + 6FeSO_4 = 2NO + 3Fe_2(SO_4)_3 + 4H_2O,$$

the gas being absorbed by the ferrous sulphate with formation of a dark-coloured, unstable compound. This is a fairly delicate test for nitrates, but is useless in presence of iodides, bromides, or nitrites.

To the neutralised acid add a small crystal of potassium iodide, a little starch mucilage, dilute sulphuric acid, and a fragment of zinc. A blue colour is gradually produced, owing to the reduction of the nitrate to nitrite, the latter liberating iodine from the hydriodic acid which is the product of the action of the sulphuric acid on the potassium iodide:

$$HNO_3 + 2H = HNO_2 + H_2O,$$
$$2HNO_2 + 2HI = I_2 + 2NO + 2H_2O.$$

This test may be used in presence of iodides and bromides.

Tests for Impurities (to be applied to the diluted acid). *Copper.*—Add excess of ammonium hydroxide and filter. The filtrate should have no blue tinge, and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—Add potassium ferrocyanide, when there should be no blue or green coloration.

Sulphate.—Add barium chloride, when no white precipitate should be formed.

Chloride, Bromate, and Iodate.—Add silver nitrate; a white precipitate soluble in ammonium hydroxide may be due to chloride, bromate, or iodate. Add a crystal of potassium iodide to a portion of the acid diluted with five times its volume of water. A pale yellow colour is imparted to the solution, but if bromate or iodate be present, a deep brown is produced, due to liberated iodine:

$$HIO_3 + 5HI = 3H_2O + 3I_2.$$

If a brown colour appears, boil the solution until purple vapours of iodine are no longer evolved, then add excess of silver nitrate solution and a slight excess of ammonium hydroxide; shake and filter. Acidify the filtrate with nitric acid, when a distinct white precipitate shows *chloride.*

NOTE.—During the manufacture of the acid, any bromate present may have been decomposed, with liberation of bromine. Add a few mils of chloroform, shake, and allow to settle. The chloroform layer should have no brown tinge.

Non-volatile Matter (Limit of).—20 grammes of the acid, evaporated to dryness in a fume-cupboard, should leave not more than 0·01 gramme of residue.

Lead Limit.—20 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—The estimation depends upon the neutralisation of the acid with N/1 sodium hydroxide solution. Weigh about 10 grammes of the acid, dilute to 100 mils, and take 20 mils for each titration, using methyl orange as indicator:

$$NaOH + HNO_3 = NaNO_3 + H_2O,$$
$$40 \equiv 63,$$
$$1000 \text{ mils N/1 } NaOH \equiv 63 \text{ grammes of } HNO_3,$$
$$1 \text{ mil N/1 } NaOH \equiv 0{\cdot}063 \text{ gramme of } HNO_3.$$

Acidum Nitricum Dilutum. *Diluted Nitric Acid.*—This contains 10 per cent by weight of HNO_3, and may be prepared by diluting 151 grammes of the official strong acid to 1000 mils with water. Specific gravity, 1·057.

Quantitative Estimation.—Weigh about 10 grammes, dilute to 100 mils and titrate portions of 20 mils with N/10 sodium hydroxide, using methyl orange as indicator.

Acidum Nitro-Hydrochloricum Dilutum. *Diluted Nitro-hydrochloric Acid.*—This is a mixture of 60 parts by volume of nitric acid, 80 parts by volume of hydrochloric acid, and 500 parts by volume of water, the whole being set aside in a glass-stoppered bottle for fourteen days before use, during which time chlorine, nitrosyl chloride, and nitrous acid are produced. Specific gravity, 1·07:

$$HNO_3 + 2HCl = Cl_2 + HNO_2 + H_2O,$$
$$HNO_3 + 3HCl = NOCl + 2H_2O + Cl_2.$$

Test for Strength.—10 mils should require about 26·6 mils of N/1 sodium hydroxide solution to neutralise the total acid present, using methyl orange as indicator.

PHOSPHORUS, P

(Atomic Wt. = 31)

The non-metallic element phosphorus occurs in Nature in the form of phosphates, notably, *apatite*, $3Ca_3(PO_4)_2,CaCl_2$, and *sombrerite*, $Ca_3(PO_4)_2$. Phosphorus is an essential element for the growth of plants, and calcium phosphate is present in most fertile soils. The hardness of bones is attributable to the 60 per cent or so of calcium phosphate which they contain.

Phosphorus occurs in several allotropic forms, the most important of these being white phosphorus and red phosphorus. White phosphorus is a waxy, crystalline solid, which on heating to 250° in the absence of air, becomes converted into the red modification. Only the white variety is official.

Preparation.—(1) The first step is the preparation of phosphoric acid. Powdered bone-ash is treated with sulphuric acid, and the clear liquid is decanted from the almost insoluble calcium sulphate:

$$Ca_3(PO_4)_2 + 3H_2SO_4 = 3CaSO_4 + 2H_3PO_4.$$

The filtrate is evaporated to a syrup, and heated in cast-iron pots with one-fourth its weight of charcoal until dry. The dried mixture is then transferred to a fireclay-lined retort, the outlet of which dips beneath the surface of water, and heated. The phosphoric acid is converted by the heat into metaphosphoric acid, with loss of water:

$$H_3PO_4 = H_2O + HPO_3,$$

and the metaphosphoric acid is reduced by the carbon, the phosphorus condensing under the water, and carbon monoxide escaping:

$$2HPO_3 + 6C = 6CO + H_2 + 2P.$$

(2) A more modern process depends upon heating a mixture of bone-ash (or mineral phosphate), finely divided silica, and coke, by means of an electric furnace. The two electrodes of the furnace project into the mass, the resistance producing intense heat. Calcium silicate and phosphorus pentoxide are formed:

$$3SiO_2 + Ca_3(PO_4)_2 = 3CaSiO_3 + P_2O_5.$$

The carbon of the coke then reduces the pentoxide, the vapours of phosphorus being led away and condensed under water:

$$P_2O_5 + 5C = 5CO + 2P.$$

PHOSPHORUS

Phosphorus

Properties and Tests for Identity.—A semi-transparent, waxy solid, usually seen in the form of cylindrical sticks, soft and flexible

at ordinary temperatures, brittle at low temperatures, and having a characteristic, disagreeable odour. Melting point, 44°. It is luminous in the dark, and on exposure to air becomes so rapidly oxidised as to burst into flame, for which reason it must always be kept under water, in which it is practically insoluble, until required for use, when small portions may be cut, rapidly dried between filter paper, and weighed (if necessary) on a watch-glass.

If phosphorus be allowed to burn in an unlimited supply of air, white vapours of phosphorus pentoxide (flowers of phosphorus) are produced, which may be condensed to form a voluminous, very hygroscopic powder :

$$4P + 5O_2 = 2P_2O_5.$$

If the supply of air be limited, however, phosphorus trioxide is formed as well :

$$4P + 3O_2 = 2P_2O_3.$$

Phosphorus is soluble 1-80 in olive oil, 1-80 in ether, 1-25 in chloroform, and 2-1 in carbon disulphide. The carbon disulphide solution on evaporation in an atmosphere of carbon dioxide leaves octahedral crystals of phosphorus. Great care must be taken if the evaporation be allowed to take place in air, since the phosphorus that remains is spontaneously inflammable.

Tests for Impurities. *Sulphur.*—Oxidise about 1 gramme of the phosphorus by boiling, very carefully and gently, in 10 mils of nitric acid diluted with 10 mils of water. The phosphorus slowly dissolves with formation of phosphoric acid, any sulphur being converted into sulphate, so that a precipitate will be obtained in the acid solution on the addition of barium chloride if sulphur be present.

Arsenic.—This is a common impurity, and may be tested for by Fleitmann's test (p. 143), excess of sodium hydroxide being added to some of the nitric acid solution prepared in the manner just described.

Oleum Phosphoratum. *Phosphorated Oil.*—This is a 1 per cent *w/w* solution of phosphorus in olive oil. The oil is heated on a sand-bath to 150° to expel all air and moisture, then cooled and filtered. The oil and phosphorus (in small pieces) are then placed in a dry stoppered bottle capable of holding rather more than the required quantity, and heated to 80° in a water-bath, shaking until solution is effected, finally adding 1 per cent of oil of lemon to flavour. The product is a clear yellow liquid, phosphorescent in the dark.

Pilula Phosphori. *Phosphorus Pill.*—A solution of phosphorus and oil of theobroma in carbon disulphide is allowed to partially evaporate, the resulting paste being made into a mass with kaolin, dried sodium sulphate, and wool fat.

The initial quantity of phosphorus is about 1 per cent of the weight of the finished mass.

PHOSPHORIC ACID, H_3PO_4

(Mol. Wt. = 98)

Derived from phosphorus pentoxide, P_2O_5, are three phosphoric acids. The direct combination of the pentoxide with water produces tribasic *orthophosphoric acid*, H_3PO_4:

$$P_2O_5 + 3H_2O = 2H_3PO_4.$$

On heating to 250° orthophosphoric acid becomes converted into tetrabasic *pyrophosphoric acid*, $H_4P_2O_7$:

$$2H_3PO_4 = H_4P_2O_7 + H_2O.$$

Pyrophosphoric acid, when heated to redness for some time, loses more water, and becomes monobasic *metaphosphoric acid*, HPO_3:

$$H_4P_2O_7 = 2HPO_3 + H_2O.$$

Of these acids, only orthophosphoric acid is official. Being a tribasic acid, it is capable of forming three series of salts, according as to whether one or more hydrogen atoms are displaced by a metal. The constitutional formulæ of certain of these compounds makes this plain:

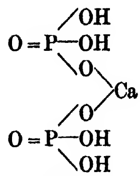
$O=P\begin{cases}OH\\OH\\OH\end{cases}$	$O=P\begin{cases}ONa\\OH\\OH\end{cases}$	$O=P\begin{cases}ONa\\ONa\\OH\end{cases}$	$O=P\begin{cases}ONa\\ONa\\ONa\end{cases}$
H_3PO_4	NaH_2PO_4	Na_2PO_4	Na_3PO_4
Ortho-phosphoric acid.	Sodium di-hydrogen phosphate.	Di-sodium hydrogen phosphate.	Normal sodium phosphate.

Di-sodium hydrogen phosphate is known in the Pharmacopœia simply as sodium phosphate, while sodium di-hydrogen phosphate is called sodium acid phosphate (pp. 78, 80). Normal sodium phosphate is not official.

It will be seen that one hydrogen atom might be displaced by one metallic radicle and another by a different one. Such a compound is microscomic salt, sodium ammonium phosphate, $NaNH_4HPO_4$:

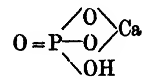
$$O=P\begin{cases}ONa\\ONH_4\\OH\end{cases}$$

A bivalent metal will be capable of displacing two hydrogen atoms, and gives rise to such a series of compounds as:



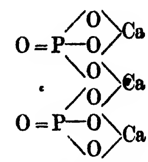
$Ca(H_2PO_4)_2$

Mono-calcium phosphate.



$CaHPO_4$

Di-calcium phosphate.



$Ca_3(PO_4)_2$

Normal calcium phosphate.

The official calcium phosphate is the normal salt (p. 104).

Preparation.—(1) Orthophosphoric acid may be prepared in t laboratory by placing in a flask fitted with a reflux condens 7 grammes of phosphorus, 50 mils of water, and 40 mils of stro nitric acid, adding the acid last, then boiling until the phosphor has disappeared. If the presence of water is not maintained tl reaction is liable to become very violent, hence the reflux co denser. When the reaction is concluded, the product may l poured into a dish and evaporated in the fume-cupboard until of syrupy consistence, in order to expel nitrous compounds and wate

(2) Phosphoric acid may also be prepared by burning phosphorus under cover, collecting the pentoxide formed, dissolving in water, then boiling with nitric acid to oxidise any lower acids of phosphorus, and concentrating as before.

(3) Commercially, the acid is made by digesting calcium phosphate with the theoretical quantity of diluted sulphuric acid, separating by decantation from the undissolved calcium sulphate, and evaporating to a syrupy consistence.

ACIDUM PHOSPHORICUM CONCENTRATUM

Concentrated Phosphoric Acid

This is required to contain 66·3 per cent by weight of orthophosphoric acid, H_3PO_4, and 33·7 per cent by weight of water.

Properties and Tests for Identity.—A colourless, syrupy liquid, with an acid taste and reaction. Specific gravity, 1·5.

On evaporation a glass-like residue is left which melts at a low red heat. The residue is sometimes known as glacial phosphoric acid, and may be obtained in sticks or slabs. It consists almost entirely of metaphosphoric acid, HPO_3.

Dilute and render alkaline with ammonium hydroxide, then add magnesia mixture,[1] when a white crystalline precipitate of

[1] Magnesia mixture may be made by mixing in a test-tube magnesium sulphate solution, ammonium chloride solution, and a few drops of strong ammonium hydroxide.

magnesium ammonium phosphate is produced, soluble in dilute acids:

$$H_3PO_4 + MgSO_4 + 3NH_4OH = NH_4MgPO_4 + (NH_4)_2SO_4 + 3H_2O.$$

To a little of the acid, diluted, add concentrated nitric acid, then an excess of ammonium molybdate solution, and warm. A canary-yellow precipitate of ammonium phosphomolybdate, $12[MoO_3] . (NH_4)_3PO_4$, is produced, soluble in ammonium hydroxide.

The neutralised acid gives with silver nitrate a yellow precipitate of silver phosphate, soluble in nitric acid and in ammonium hydroxide.

The neutralised acid gives with ferric chloride a yellowish-white precipitate of ferric phosphate, soluble in excess of the chloride and in dilute mineral acids, but insoluble in acetic acid.

Tests for Impurities (to be applied to the diluted acid). *Copper.*—Add excess of ammonium hydroxide and filter. The filtrate should have no blue tinge, and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—Add nitric acid and potassium ferrocyanide solution. Not more than a slight blue or green colour should be produced.

Calcium and Magnesium.—If a white precipitate is obtained on addition of excess of ammonium hydroxide, it may contain either or both of these metals as phosphates. Filter off the precipitate, dissolve in dilute hydrochloric acid, remove the phosphate by the method described in the Appendix (p. 424), and test the resulting solution as follows. Make alkaline with ammonium hydroxide, and add ammonium carbonate, when there should be no white precipitate (absence of calcium). Filter, if necessary, and add sodium phosphate. There should be no precipitate, immediately or on standing (absence of magnesium).

Sulphate.—Dilute well, add nitric acid, then barium chloride. Not more than a slight turbidity should be produced.

Chloride.—Dilute well, add nitric acid, then silver nitrate. There should be no more than a faint opalescence.

Nitrate and Nitrite.—When a cold solution of ferrous sulphate is carefully poured on to the surface of a cooled mixture of the acid with an equal volume of sulphuric acid, no brown ring should develop at the junction of the liquids (p. 35).

Phosphorous Acid.—A 1-5 dilution should give no turbidity with mercuric chloride solution.

Metaphosphoric Acid.—This impurity would cause the coagulation of albumin on shaking in a test-tube.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—The volumetric test for phosphoric acid forms an interesting and instructive exercise. It has already been shown (p. 39) that phosphoric acid is tribasic—the molecule contains three atoms of hydrogen, each or all of which may be displaced by metals forming a series of salts. The estimation depends upon the effect of these salts on indicators. If normal

sodium hydroxide solution be run from a burette, drop by drop, into a little phosphoric acid containing methyl orange, the colour of the indicator changes from red to yellow when sufficient alkali has been supplied to convert all the acid into sodium di-hydrogen phosphate :

$$NaOH + H_3PO_4 = NaH_2PO_4 + H_2O.$$

If now, a few drops of phenolphthalein be added, and titration continued, a red colour is produced when such additional quantity of alkali has been added as will convert the di-hydrogen salt into the di-sodium salt :

$$NaOH + NaH_2PO_4 = Na_2HPO_4 + H_2O.$$

In other words, sodium di-hydrogen phosphate is neutral to methyl orange, but acid to phenolphthalein, whereas di-sodium hydrogen phosphate is alkaline to methyl orange, but neutral to phenolphthalein. The quantity of alkali used in each stage should be the same, and this affords a useful check, since the quantity of acid present may be calculated from either reading.

Weigh about 10 grammes of phosphoric acid, and dilute to 100 mils. Take 20 mils for each titration, add a few drops of methyl orange and titrate with N/1 sodium hydroxide until the colour changes from red to yellow, and notice the volume of alkali used. Next, add a little phenolphthalein and about 20 mils of 1-4 sodium chloride solution—this to give a sharper end-point—and continue to titrate until a permanent red colour is obtained. Again notice the volume of alkali used, which should be the same as in the methyl orange titration. The acid present may now be calculated from the total number of mils of alkali required :

$$\begin{gathered} 2NaOH + H_3PO_4 = Na_2HPO_4 + 2H_2O, \\ 2 \times 40 \equiv 98 \\ 1000 \text{ mils N/1 } NaOH \equiv 49 \text{ grammes of } H_3PO_4, \\ 1 \text{ mil N/1 } NaOH \equiv 0{\cdot}049 \text{ gramme of } H_3PO_4. \end{gathered}$$

Acidum Phosphoricum Dilutum. *Diluted Phosphoric Acid.*—This contains 10 per cent by weight of H_3PO_4, and may be prepared by diluting 159·5 grammes of the concentrated acid to 1000 mils. Specific gravity, 1·057.

Quantitative Estimation.—It is estimated as just described under Acidum Phosphoricum Concentratum. Weigh about 10 grammes of the acid, dilute to 100 mils, and take 20 mils for each titration, using N/10 sodium hydroxide.

CHAPTER V

COMPOUNDS OF BORON AND SILICON

THE non-metallic elements boron and silicon have a few points in common, although they are placed in different families in the Periodic Classification of elements, boron being tervalent and silicon quadrivalent. The number of their compounds used in pharmacy is small, but such as are used are common and important substances.

COMPOUNDS OF BORON

B (Atomic Wt. = 11)

The element boron does not occur in the free state, but in combination with hydrogen and oxygen in the form of boric acid, H_3BO_3, as *tincal*, the sodium salt of tetraboric acid (crude borax), and as native calcium borate.

When boron is burned in air it forms boron trioxide, B_2O_3, which on exposure to moisture becomes converted into *orthoboric acid*:

$$3H_2O + B_2O_3 = 2H_3BO_3.$$

On heating to 100°, orthoboric acid loses water, and yields *metaboric acid*:

$$2H_3BO_3 = 2HBO_2 + 2H_2O.$$

On further heating to 160° more water is driven off, leaving *tetraboric acid* (sometimes called pyroboric acid):

$$4HBO_2 = H_2B_4O_7 + H_2O,$$

and at a red heat, the whole of the water is expelled, leaving the trioxide:

$$H_2B_4O_7 = 2B_2O_3 + H_2O.$$

ORTHOBORIC ACID, H_3BO_3

(Mol. Wt. = 62)

Preparation.—(1) Boric acid occurs naturally in volcanic jets of steam issuing from the ground in Tuscany. The steam condenses in natural or artificial lagoons, the liquid in which is concentrated

by utilising the heat of the steam, crude boric acid crystallising out. The crude acid, which is yellow in colour, is purified by dissolving in water, mixing with freshly ignited charcoal, filtering, and recrystallising.

(2) Boric acid may be prepared in the laboratory by precipitation from an aqueous solution of borax, by means of a mineral acid. Dissolve about 30 grammes of borax in 80 mils of water by aid of heat; mix about 6 mils of concentrated sulphuric acid with 30 mils of water, and add the diluted acid to the borax solution; filter while hot, set aside to crystallise, and again filter. Wash the crystals on the filter with cold water until the washings are free from sulphate, then dry between filter paper on a porous plate. If a sample of special purity be required, the boric acid may be dissolved in hot alcohol and recrystallised:

$$Na_2B_4O_7 + 5H_2O + H_2SO_4 = Na_2SO_4 + 4H_3BO_3.$$

It is often difficult to obtain a clear solution of borax on boiling and filtering, but this may be overcome by adding to the hot liquid, prior to the addition of the sulphuric acid, a small quantity of white of egg mixed with a little water, when the coagulation of the albumen retains the insoluble particles. The use of hydrochloric acid instead of sulphuric acid gives a larger yield, and the crystals are more quickly washed, but they seem to lack the pearly appearance characteristic of a good sample.

ACIDUM BORICUM

Boric Acid. *Syn.* Boracic Acid

This is required to contain not less than 99·5 per cent of H_3BO_3.

Properties and Tests for Identity.—White, pearly, lamellar crystals, separate, or in masses, or in the form of a white, odourless powder, unctuous to the touch, with a taste that is at first bitter and slightly acid, but afterwards sweetish. Soluble 1-25 in water, and 1-3 in boiling water, 1-4 in glycerin, and 1-30 in alcohol, the crystals giving a clearer solution than the powder.

Place some boric acid in an evaporating dish, add a little alcohol, or methylated spirit, and ignite. The edge of the flame will be seen to be tinged with green, owing to the formation of volatile ethyl borate. Make an aqueous solution and test, (*a*) with blue litmus paper, when a claret-red colour is produced, and (*b*) with turmeric paper slightly acidified with hydrochloric acid, when a brown colour is produced, which becomes greenish-black on moistening with potassium hydroxide solution. The brown colour produced by boric acid with turmeric paper differs from that produced by alkalies in not being discharged by acids.

Carefully heat a little boric acid. It first fuses, then swells, and on strongly heating becomes converted into a transparent, hygroscopic mass of boric oxide.

Tests for Impurities (tests for metallic impurities to be applied to a solution in dilute hydrochloric acid). *Copper.*—Add excess of ammonium hydroxide and filter. The filtrate should have no blue tinge and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—There should be no more than the slightest blue or green colour on the addition of nitric acid followed by potassium ferrocyanide solution.

Calcium.—Add ammonium chloride, excess of ammonium hydroxide, and ammonium oxalate, when there should be no distinct precipitate.

Magnesium.—Add ammonium chloride, ammonium hydroxide in excess, then sodium phosphate. There should be no precipitate on standing for a short time.

Chloride.—To the aqueous solution add nitric acid and silver nitrate. There should be no more than a faint opalescence.

Sulphate.—Add to the aqueous solution hydrochloric acid, and test with barium chloride. There should be no more than a slight turbidity.

Lead Limit.—25 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—Boric acid is estimated by titration with sodium hydroxide in presence of glycerin. It is too feeble an acid to affect methyl orange, and when phenolphthalein is used as indicator, the red colour appears before all the acid is neutralised, owing to the partial hydrolysis of the sodium metaborate, which is the compound formed by the reaction:

$$NaOH + H_3BO_3 = NaBO_2 + 2H_2O.$$

The glycerin is said to prevent the reaction proceeding in the reverse direction. Another suggestion is that a glyceryl borate is formed which is a sufficiently strong acid to give a sharp end-point with phenolphthalein. Weigh about 4 grammes of the acid, dissolve in sufficient water to produce 100 mils, and take 20 mils, with an equal volume of glycerin, for each titration, using N/1 sodium hydroxide, and phenolphthalein as indicator:

$$NaOH + H_3BO_3 = NaBO_2 + 2H_2O,$$
$$40 \doteq 62$$
$$1000 \text{ mils N/1 NaOH} \doteq 62 \text{ grammes of } H_3BO_3,$$
$$1 \text{ mil N/1 NaOH} \doteq 0{\cdot}062 \text{ gramme of } H_3BO_3.$$

Glycerinum Acidi Borici. *Glycerin of Boric Acid.*—This is a solution of the ester, glyceryl borate, in glycerin. Glycerin and boric acid are heated in a tared dish on a sand-bath until the weight has been reduced to a definite amount, the boric acid combining with the glycerin to produce glyceryl borate and water:

$$C_3H_5(OH)_3 + H_3BO_3 = C_3H_5BO_3 + 3H_2O.$$

The reaction is a reversible one, the water being capable of hydrolysing some of the ester; hence the evaporation to a definite weight, which indicates that the water has been driven off by heat, the hydrolysis thus being prevented. The temperature must not rise above 150°, or decomposition of the glycerin may occur, with formation of acrolein (p. 283). The contents of the dish are now dissolved in glycerin, which should be previously warmed, as otherwise the ester is cooled to solidification, when it is difficult to dissolve.

SODIUM TETRABORATE, $Na_2B_4O_7,10H_2O$

(Mol. Wt. = 382)

The sodium salt of tetraboric acid—usually termed borax—occurs to about 52 per cent in the mineral *tincal*, which is found in the dried-up inland lakes of California, India, and Tibet; but most of the borax of commerce is obtained by decomposing native calcium borate, which forms large deposits in Bolivia.

Preparation.—(1) The powdered calcium borate is boiled with water, and sodium carbonate added, the calcium being precipitated as carbonate, and a mixture of sodium tetraborate and metaborate remaining in solution:

$$Ca_2B_6O_{11} + 2Na_2CO_3 = 2CaCO_3 + Na_2B_4O_7 + 2NaBO_2.$$

On cooling, the borax crystallises out, while the more soluble metaborate remains dissolved. The mother liquor is concentrated further, and carbon dioxide passed through the solution, with formation of more borax, which is precipitated in the form of fine crystals:

$$2Na_2B_2O_4 + CO_2 = Na_2CO_3 + Na_2B_4O_7.$$

(2) Borax may be prepared in the laboratory by adding the theoretical quantity of anhydrous sodium carbonate to a boiling solution of boric acid. On cooling, the borax crystallises in the form of transparent prisms:

$$4H_3BO_3 + Na_2CO_3 = Na_2B_4O_7 + 6H_2O + CO_2.$$

BORAX PURIFICATUS

Purified Borax. *Syn.* Biborate of Sodium

This is required to contain not less than 98·9 per cent of sodium pyroborate (tetraborate), $Na_2B_4O_7,10H_2O$.

Properties and Tests for Identity.—Colourless, transparent prisms, often efflorescent. Taste, saline and alkaline. Soluble 1·25 in water, 2·1 in boiling water, 1·1 in glycerin. The aqueous solution

has an alkaline reaction owing to hydrolysis. In concentrated solution, hydrolysis is only partial:

$$Na_2B_4O_7 + 3H_2O = 2NaBO_2 + 2H_3BO_3,$$

but on further dilution, hydrolysis may be nearly complete:

$$NaBO_2 + 2H_2O = H_3BO_3 + NaOH,$$

and the emulsifying action of borax on oils may be attributed to the presence of the free alkali.

Heated on a platinum wire in the bunsen flame, an intense yellow colour is imparted to the flame (presence of sodium). The salt fuses, swells, then loses water, and, finally, forms a clear bead of anhydrous borax, which, on dipping into salts of some metals that form coloured oxides, and again heating, assumes characteristic colours, the colour depending upon the metal present, and whether the bead is heated in the oxidising or the reducing portion of the flame. This characteristic behaviour may be explained by the assumption that anhydrous borax contains an acid anhydride, $2NaBO_2 . B_2O_3$, and that the metallic oxide combines with the B_2O_3 to form a metaborate, thus:

$$Na_2B_4O_7 + CuO = Cu(BO_2)_2 + 2NaBO_2.$$

Moisten a little borax with sulphuric acid in an evaporating basin, add a little alcohol or methylated spirit, ignite, and stir with a glass rod. The edge of the flame is tinged with green, due to the liberation of boric acid (p. 44).

To a saturated solution, add hydrochloric acid. A white crystalline precipitate of boric acid is produced which may be tested with turmeric paper (p. 44).

Tests for Impurities. *Copper.*—To the aqueous solution add ammonium hydroxide and filter. The filtrate should have no blue tinge, and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—A dilute aqueous solution, acidified with nitric acid, should yield no blue or green colour with potassium ferrocyanide.

Calcium.—An aqueous solution should give no white precipitate on the addition of ammonium chloride, ammonium hydroxide and ammonium oxalate.

Carbonate and Bicarbonate.—The aqueous solution should not effervesce with acids.

Sulphate.—A 1-50 solution, acidified with hydrochloric acid, should give no more than a slight turbidity with barium chloride.

Chloride.—A 1-50 solution, acidified with nitric acid, should give no more than a faint opalescence with silver nitrate.

Lead Limit.—5 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—It has been shown (p. 44) that the addition of acid to borax results in the liberation of boric acid, and the formation of the sodium salt of the acid used. If the borax

is titrated with standard acid, using methyl orange as indicator, neutrality is shown when all the boric acid is set free, because boric acid has no effect on methyl orange.

$$Na_2B_4O_7 + H_2SO_4 + 5H_2O = Na_2SO_4 + 4H_3BO_3.$$

If phenolphthalein and glycerin are now added, the free boric acid can be titrated as described under Acidum Boricum ; and from the fact that one molecule of borax will yield four molecules of boric acid, the amount of borax present in the sample under examination can be calculated. It will be seen that this method shows the amounts of total alkali and total boric acid present—a useful check, for if the borax contained alkaline impurity, titration with acid only would still give a high percentage result.

Weigh about 2 grammes of borax and dissolve in water. Titrate with N/1 sulphuric acid, using methyl orange as indicator ; then add about an equal volume of glycerin and a few drops of phenolphthalein and titrate the released boric acid with N/1 sodium hydroxide. If the sample is a correct one, containing no excess of boric acid or of alkali, the volume of normal alkali required should be exactly twice that of normal acid used in the first titration, because one molecule of sulphuric acid, which is dibasic, is equivalent to one molecule of borax, but one molecule of borax is equivalent to four molecules of sodium hydroxide :

$$NaOH + H_3BO_3 = NaBO_2 + 2H_2O,$$
$$Na_2B_4O_7,10H_2O \text{ yields } 4H_3BO_3,$$
$$\therefore\ 4NaOH \equiv 4H_3BO_3 \equiv Na_2B_4O_7,10H_2O,$$
$$4 \times 1000 \text{ mils N/1 NaOH} \equiv 382 \text{ grammes } Na_2B_4O_7,10H_2O,$$
$$1 \text{ mil N/1 NaOH} \equiv 382/4 = 95{\cdot}5 \text{ grammes } Na_2B_4O_7,10H_2O,$$

or calculating from the first titration only :

$$H_2SO_4 \equiv Na_2B_4O_7,10H_2O,$$
$$98 \equiv 382,$$
$$1000 \text{ mils N/1 } H_2SO_4 \equiv 191 \text{ grammes } Na_2B_4O_7,10H_2O,$$
$$1 \text{ mil N/1 } H_2SO_4 \equiv 0{\cdot}191 \text{ gramme } Na_2B_4O_7,10H_2O.$$

Glycerinum Boracis. *Glycerin of Borax.*—A solution of borax in glycerin. The product effervesces slightly with sodium bicarbonate, and it may be assumed that the glycerin reacts with the borax to produce sodium metaborate, and glyceryl borate ; the glyceryl borate then being partially hydrolysed by the water, and boric acid set free :

$$2C_3H_5(OH)_3 + Na_2B_4O_7,10H_2O = 2C_3H_5BO_3 + 2NaBO_2 + 13H_2O,$$
$$C_3H_5BO_3 + 3H_2O = C_3H_5(OH)_3 + H_3BO_3.$$

COMPOUNDS OF SILICON

Si (Atomic Wt. = 28)

The compounds of silicon are seldom used in medicine, but two of them, talc and kaolin, are common substances, constantly

used in pharmaceutical operations. Kaolin is also used as a medicament.

KAOLIN, $Al_2H_2Si_2O_8,H_2O$.

This substance, often termed china, or porcelain, clay, is derived from the decomposition of the felspar of granitic rocks, and occurs in large quantities in Cornwall. It consists largely of an aluminium silicate with traces of aluminium hydroxide, magnesium oxide, calcium carbonate, and ferric oxide. Fuller's earth is an impure variety of kaolin.

Purification.—Kaolin is purified for pharmaceutical purposes by washing with hydrochloric acid to remove calcium carbonate, and then with sulphuric acid to dissolve other impurities. It is finally washed with water to remove chlorides and sulphates, and freed from gritty particles by elutriation (p. 101).

KAOLINUM

Kaolin

Properties and Tests for Identity.—A soft, whitish powder with an earthy taste, insoluble in water and darkening in contact with it, and insoluble in dilute acids.

On fusion with alkalies, alkaline silicates and aluminates are formed. The fused mass is partially or completely soluble in water, and if digested with water and filtered, the filtrate, on acidification with hydrochloric acid, deposits hydrated silica. If this be filtered off, and excess of ammonium hydroxide added to the filtrate, a precipitate of aluminium hydroxide is obtained.

Tests for Impurities. *Iron.*—Shake with dilute hydrochloric acid and filter. The filtrate should not give more than a very slight reaction for iron on testing with potassium ferrocyanide.

Carbonate.—There should be no effervescence on the addition of acids.

Volatile Matter (Limit of).—Not less than 85 per cent of residue should remain after ignition at a red heat.

TALC

Syn. French Chalk ; Creta Gallica ; Soapstone

This substance is not official, but is mentioned in Appendix I. of the Pharmacopœia. It is a native hydrated silicate of magnesium.

Purification.—For pharmaceutical purposes, talc should be purified as follows: Mix the talc, in fine powder, with five times its weight of boiling water and one-tenth its weight of hydrochloric acid. Boil for fifteen minutes, then set aside for fifteen minutes and decant the supernatant liquid. Repeat this treatment, using the same quantity of water, but only half the amount of acid.

Decant the liquid and wash the residue with water, first by decantation, and afterwards on a linen strainer until free from chloride.

Properties and Tests for Identity.—It occurs either in the form of a fine, white, tasteless powder, imparting a feeling of soapiness to the skin, or in the form of greenish-grey irregular masses with a waxy lustre.

Fuse with anhydrous sodium carbonate and potassium carbonate, and digest the residue with hot water. Filter, add a slight excess of sulphuric acid to the filtrate, and evaporate to dryness. Add water to the residue, boil, and filter. An insoluble residue of silica remains on the filter. To the filtrate, add ammonium chloride and ammonium hydroxide, when a white precipitate of aluminium hydroxide is formed. Filter, add sodium phosphate solution to the filtrate, shake, and set aside. A white precipitate is formed (magnesium).

CHAPTER VI

COMPOUNDS OF POTASSIUM, SODIUM, LITHIUM, AND AMMONIUM

COMPOUNDS OF POTASSIUM

K (Atomic Wt. = 39)

THESE are generally white or colourless, and are, with very few exceptions, easily soluble in water, the solution in many cases having an alkaline reaction owing to hydrolysis. The salts can be prepared by acting upon the hydroxide or the carbonate with the appropriate acid, or by a process of double decomposition with the salt of another metal.

Potassium compounds are principally obtained from the enormous "salt-beds" in the neighbourhood of Stassfurt (Saxony), wherein are found the minerals *sylvine*, KCl; *carnallite*, $KCl, MgCl_2,6H_2O$; *kainite*, $K_2SO_4,MgSO_4,MgCl_2,6H_2O$, and others.

General Tests for Potassium.—(1) Potassium compounds impart a lilac coloration to the bunsen flame, but in the presence of sodium the colour may be masked, in which case the flame must be viewed through an indigo prism, when the potassium flame is seen as crimson, the yellow colour of the sodium flame being cut off.

Salts of lead, arsenic, antimony, and other metals give bluish flame colorations. It is necessary, therefore, to remove such metals before testing for potassium.

(2) Hydrogen platinichloride, added to a solution of a potassium salt, gives a yellow crystalline precipitate of potassium platinichloride, insoluble in alcohol:

$$2KNO_3 + H_2PtCl_6 = K_2PtCl_6 + 2HNO_3.$$

Owing to the high cost of the reagent this test should be omitted unless essential, and even then it should be carried out only on a watch-glass.

(3) A strong solution of tartaric acid, added to a concentrated solution of a potassium salt, yields, when well shaken and allowed to stand, a white crystalline precipitate of potassium hydrogen tartrate:

$$H_2C_4H_4O_6 + KNO_3 = KHC_4H_4O_6 + HNO_3.$$

POTASSA CAUSTICA

Potassium Hydroxide, KOH. (Mol. Wt. = 56.)
Syn. Caustic Potash

This is required to contain not less than 85 per cent of KOH.

Preparation.—(1) Potassium hydroxide is manufactured by the electrolysis of a solution of potassium chloride:

$$\begin{cases} 2KCl = 2K + Cl_2, \\ 2K + 2H_2O = 2KOH + H_2. \end{cases}$$

Chlorine escapes at the anode and potassium hydroxide collects at the cathode. The liquid is evaporated to dryness, and the resulting fused potassium hydroxide is run into moulds to form the familiar sticks.

(2) Another method consists in boiling a solution of potassium carbonate with milk of lime:

$$K_2CO_3 + Ca(OH)_2 = CaCO_3 + 2KOH.$$

The reaction is at an end when all the potassium carbonate has been decomposed, as shown by the fact that a little of the clear liquid no longer effervesces when tested with hydrochloric acid. The precipitated calcium carbonate is allowed to settle, and the supernatant liquid decanted and evaporated. It is essential for the successful performance of this process that the solution shall be kept dilute, since otherwise there is a tendency for the reaction to proceed in the reverse direction.

Purification.—Commercial potassium hydroxide is liable to contain considerable quantities of carbonate and other impurities, from which it may be freed by dissolving in alcohol and filtering, the solvent being recovered by distillation. The product is very pure and is known as "potash by alcohol".

Properties.—It occurs in hard, white, deliquescent sticks, alkaline, and very corrosive. Soluble 2·1 in water, and 1·3 in alcohol (90 per cent). When strongly heated it melts without decomposition.

Tests for Impurities. *Insoluble Solids.*—1 gramme should leave practically no residue in 2 mils of water or in 19 mils of alcohol (90 per cent).

Copper.—Acidify the aqueous solution with hydrochloric acid, add excess of ammonium hydroxide, and filter. The filtrate should have no blue tinge, and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Lead.—To the aqueous solution add ammonium hydroxide, potassium cyanide, and a few drops of sodium sulphide solution. There should be no dark coloration.

Arsenic.—This should be completely absent. (Apply Fleitmann's Test, p. 143.)

Aluminium.—Neutralise with hydrochloric acid, add ammonium

chloride and ammonium hydroxide, and boil, when no appreciable white precipitate should be formed.

Calcium.—Add to the aqueous solution ammonium oxalate. There should be no white precipitate.

Silica.—Dissolve in water, acidify with hydrochloric acid, and evaporate to dryness. Any silicate will be converted into insoluble silica, and will remain as a residue on boiling with water.

Carbonate.—There should be no marked effervescence on the addition of acids to the aqueous solution.

Quantitative Estimation.—Potassium hydroxide is estimated by neutralisation with standard acid. Weigh about 5 grammes in a stoppered weighing bottle, and dissolve in sufficient water to produce 100 mils. Titrate portions of 20 mils with N/1 sulphuric acid, using methyl orange as indicator :-

$$H_2SO_4 + 2KOH = K_2SO_4 + 2H_2O,$$
$$98 = 2 \times 56,$$
$$1000 \text{ mils } N/1\ H_2SO_4 = 56 \text{ grammes KOH},$$
$$1 \text{ mil } N/1\ H_2SO_4 = 0{\cdot}056 \text{ gramme KOH}.$$

Note.—This estimation gives the total alkali (potassium hydroxide and carbonate) in the sample, calculated as hydroxide. If it is desired to estimate the amount of carbonate present, the above titration is repeated, using phenolphthalein as indicator. In this case the phenolphthalein colour disappears when the total potassium hydroxide has been neutralised and the carbonate has been converted into bicarbonate :

$$2K_2CO_3 + H_2SO_4 = K_2SO_4 + 2KHCO_3.$$

The difference between the methyl orange and the phenolphthalein titrations corresponds, therefore, to half the carbonate present.

LIQUOR POTASSÆ

Solution of Potash

This is a 5 per cent *w/v* solution of potassium hydroxide in water. It should be stored in green glass bottles, since the alkali has a solvent action on the lead of white glass. The bottle should be fitted with a glass stopper to prevent the access of atmospheric carbon dioxide, and the stopper should be smeared with soft paraffin, as otherwise the alkali may render it immovable. Specific gravity, 1·045.

Tests for Impurities. *Lead, Copper, Arsenic.*—Test as under Potassa Caustica.

Iron.—Acidify with nitric acid and add potassium ferrocyanide, when there should be no blue or green colour.

Aluminium and Calcium.—Test as under Potassa Caustica.

Magnesium.—Add ammonium hydroxide and sodium phosphate, shake, and allow to stand. There should be no white precipitate.

Ammonium.—The solution should not evolve ammonia on boiling, detected by its odour, and by turmeric paper (p. 32).

Sodium.—Evaporate a little of the solution almost to dryness, add hydrochloric acid to the residue, and apply the flame test, when no pronounced and continuous yellow colour should be obtained.

Carbonate.—There should be no appreciable effervescence with acids.

Sulphate.—Add excess of hydrochloric acid, and test with barium chloride. There should not be more than a slight turbidity.

Chloride.—Add excess of nitric acid, and test with silver nitrate. There should not be more than a slight opalescence.

Quantitative Estimation.—It is estimated as described under Potassa Caustica, employing 20 mils for each titration.

POTASSII CARBONAS

Potassium Carbonate, K_2CO_3. (Mol. Wt. = 138.)
Unofficial Syn. Salt of Tartar

This is required to contain not less than 81·5 per cent of K_2CO_3.

Preparation.—(1) Potassium carbonate may be obtained by lixiviating with water the ashes of various plants. The product of this process was formerly termed " pot-ashes ", whence the origin of the term potash.

(2) Potassium carbonate is prepared also by reducing potassium sulphate (obtained from deposits of potassium salts in the region of Stassfurt) to sulphide with carbon, and then heating with calcium carbonate, a method similar to the Le Blanc process for the preparation of sodium carbonate (p. 70).

(3) Pure potassium carbonate may be obtained by heating the bicarbonate until all evolution of carbon dioxide has ceased :

$$2KHCO_3 = K_2CO_3 + H_2O + CO_2,$$

or by igniting potassium hydrogen tartrate, extracting the charred mass with water, filtering, and evaporating :

$$2KHC_4H_4O_6 = K_2CO_3 + 3C + 5H_2O + 4CO.$$

Purification.—The pure substance may be obtained from crude potash by dissolving in an equal weight of water, allowing to stand for a day or two, filtering, and evaporating the filtrate to dryness, the solid being manipulated towards the end to induce granulation.

Properties.—A white, crystalline or granular, deliquescent powder, odourless, with a strongly alkaline taste and reaction. Soluble 1-1 in water, insoluble in alcohol. The crystals contain three molecules of water, which they lose at 130° ; the anhydrous salt melts at a red heat without decomposition.

Tests for Impurities. *Limit of Water.*—Loses not more than 18·5 per cent of its weight on heating to redness.

Copper.—Dissolve in dilute hydrochloric acid, add excess of ammonium hydroxide, and filter. The filtrate should have no blue tinge, and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—Dissolve in slight excess of dilute nitric acid and add potassium ferrocyanide. Not more than the slightest blue or green colour should be observed.

Aluminium.—Dissolve in dilute nitric acid, add excess of sodium hydroxide solution, filter off any precipitate of iron, add to the filtrate excess of ammonium chloride, and boil. No flocculent white precipitate should be produced.

Calcium.—Dissolve in excess of hydrochloric acid, make alkaline with ammonium hydroxide, and test with ammonium oxalate. There should be no precipitate.

Magnesium.—Dissolve in excess of hydrochloric acid, make alkaline with ammonium hydroxide, and add sodium phosphate. No precipitate should appear even on shaking and allowing to stand.

Sodium.—Apply the flame test.

Nitrate.—Neutralise an aqueous solution with sulphuric acid, and apply the brown-ring test (p. 35).

Sulphate.—Render the aqueous solution acid with hydrochloric acid, and test with barium chloride. There should be no precipitate.

Sulphide.—Add excess of dilute hydrochloric acid to the dry substance and test the evolved gas with lead acetate paper, which should not be darkened.

Thiosulphate.—On acidification the aqueous solution should yield no precipitate of sulphur, and no odour of sulphur dioxide.

Chloride and Cyanide.—If the aqueous solution, made acid with nitric acid, yields a white precipitate soluble in ammonia on the addition of silver nitrate, either chloride or cyanide may be present.

Acidify an aqueous solution with nitric acid and boil until any hydrocyanic acid is expelled. Add silver nitrate, when no more than an opalescence should be produced (absence of more than traces of chloride). To a fresh portion of the aqueous solution add sodium hydroxide, a little ferrous sulphate, and a drop of ferric chloride; boil and acidify with dilute hydrochloric acid. No blue or green coloration should be produced (absence of cyanide).

Lead Limit.—5 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—Potassium carbonate is estimated by neutralisation with sulphuric acid. Weigh and dissolve about 5 grammes in sufficient water to produce 100 mils. Titrate portions of 20 mils with N/1 sulphuric acid, using methyl orange as indicator:

$$H_2SO_4 + K_2CO_3 = K_2SO_4 + CO_2 + H_2O,$$
$$98 = 138,$$
$$1000 \text{ mils N/1 } H_2SO_4 = 69 \text{ grammes } K_2CO_3,$$
$$1 \text{ mil N/1 } H_2SO_4 \equiv 0{\cdot}069 \text{ gramme } K_2CO_3.$$

POTASSII BICARBONAS

Potassium Bicarbonate, $KHCO_3$. (Mol. Wt. = 100)

This is required to contain not less than 99 per cent of $KHCO_3$.

Preparation.—The bicarbonate may be prepared by saturating a solution of the carbonate with carbon dioxide, and evaporating to crystallisation at a temperature not exceeding 70°:

$$K_2CO_3 + CO_2 + H_2O = 2KHCO_3.$$

Owing to the fact that potassium bicarbonate is readily soluble in water, it is not practicable to manufacture it by any method analogous to the Solvay process for sodium bicarbonate.

Properties.—Colourless crystals, or a crystalline powder, not deliquescent. It has a saline taste, and is alkaline to methyl orange. Soluble 1-4 in water, almost insoluble in alcohol (90 per cent). On heating the aqueous solution carbon dioxide is evolved, and the bicarbonate becomes converted into carbonate.

Twenty grammes are neutralised by 14 of citric acid and 15 of tartaric acid.

Distinction between Potassium Carbonate and Bicarbonate.—(1) Add the dry substance to boiling water; carbon dioxide is evolved from the bicarbonate.

(2) Dissolve in cold water and add magnesium sulphate. A white precipitate is obtained immediately in the case of the carbonate, but in the case of the bicarbonate, only on boiling.

Tests for Impurities. *Copper.*—Dissolve in dilute hydrochloric acid, add excess of ammonium hydroxide, and filter. The filtrate should have no blue tinge, and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—Dissolve in slight excess of dilute nitric acid and test with potassium ferrocyanide, when there should be no more than a slight green or blue tinge.

Sodium.—Apply the flame test.

Sulphate.—Dissolve in excess of dilute hydrochloric acid and add barium chloride. There should be no turbidity.

Chloride.—Dissolve in excess of nitric acid and test with silver nitrate. There should be no more than an opalescence.

Lead Limit.—5 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—(1) Weigh about 1 gramme and ignite to a dull red heat in a crucible, allow to cool in a desiccator, and again weigh. From the weight of the residue, calculate the amount of bicarbonate originally present.

$$2KHCO_3 = K_2CO_3 + H_2O + CO_2.$$
$$2 \times 100 \text{ grammes} \equiv 138 \text{ grammes}.$$

(2) It is also estimated by neutralisation with standard acid. Weigh about 5 grammes of potassium bicarbonate, dissolve in cold

water, and dilute to 100 mils. Titrate portions of 20 mils with N/1 sulphuric acid, using methyl orange as indicator:

$$H_2SO_4 + 2KHCO_3 = K_2SO_4 + 2H_2O + 2CO_2,$$
$$98 \equiv 2 \times 100,$$
$$1000 \text{ mils N/1 } H_2SO_4 \equiv 100 \text{ grammes of } KHCO_3,$$
$$1 \text{ mil N/1 } H_2SO_4 \doteq 0{\cdot}100 \text{ gramme of } KHCO_3.$$

(3) *Potassium Carbonate and Bicarbonate.*—It may be required to estimate the proportion of carbonate and bicarbonate present in a mixture of these substances. If such a mixture be titrated with sulphuric acid, the first reaction that takes place is the conversion of all the carbonate into bicarbonate :

$$2K_2CO_3 + H_2SO_4 = K_2SO_4 + 2KHCO_3.$$

At this point the solution is neutral to phenolphthalein, but alkaline to methyl orange. If more sulphuric acid is run in now, all the bicarbonate originally present, together with that formed from the carbonate, is converted into potassium sulphate, the solution then being neutral to both indicators:

$$2KHCO_3 + H_2SO_4 = K_2SO_4 + 2H_2O + 2CO_2.$$

Weigh about 5 grammes, dissolve in cold water, and dilute to 100 mils. Slowly titrate portions of 20 mils with N/1 sulphuric acid, using phenolphthalein as indicator, and record the reading. Then add a few drops of methyl orange to the same solution and continue to titrate, recording the second reading. The volume of acid used in the phenolphthalein titration corresponds to half the carbonate present. This volume, doubled, and subtracted from the total quantity of acid used, will give the amount of acid required for the bicarbonate originally present.

POTASSII BROMIDUM

Potassium Bromide, KBr. (Mol. Wt. = 119)

This is required to contain not less than 98 per cent of KBr when dried at 100°.

Preparation.—(1) Iron borings are treated with bromine, yielding a bromide of iron. This is then boiled with potassium carbonate solution, filtered, and the filtrate evaporated to crystallisation:

$$Fe_3Br_8 + 4K_2CO_3 = Fe_3O_4 + 8KBr + 4CO_2.$$

(2) It is formed when bromine, in slight excess, is added to a concentrated potassium hydroxide solution. The solution, which also contains potassium bromate, is evaporated to dryness, ignited with charcoal to reduce the bromate to bromide, treated with water and filtered. The filtrate is then evaporated to crystallisation:

$$6KOH + 3Br_2 = 5KBr + KBrO_3 + 3H_2O,$$
$$KBrO_3 + 3C = KBr + 3CO.$$

Properties.—Colourless, cubical, anhydrous crystals, with a saline taste. Soluble 1·2 in water, and 1·200 in alcohol (90 per cent). On heating it melts without decomposition.

Tests for Impurities (to be applied to the aqueous solution). *Copper.*—Add excess of ammonium hydroxide and filter. The filtrate should have no blue tinge and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—Add dilute nitric acid and potassium ferrocyanide, when there should be no blue or green colour.

Barium and Calcium.—Add ammonium chloride, ammonium hydroxide, and ammonium carbonate. If a precipitate be produced, examine by Table on p. 424.

Magnesium.—Add ammonium chloride, ammonium hydroxide, and sodium phosphate. There should be no precipitate, even on shaking and allowing to stand.

Carbonate.—There should be no effervescence with dilute acid.

Sulphate.—Acidify strongly with hydrochloric acid and add barium chloride. There should not be more than a slight turbidity.

Chloride.—This, though not mentioned in the Pharmacopœia, is one of the most common impurities, some American samples of bromide containing as much as 5 per cent of potassium chloride. Ignite in a crucible, in order to convert any bromate and iodate present into bromide and iodide; allow to cool, dissolve in dilute nitric acid, and boil in order to oxidise the bromide, and any iodide, to bromine and iodine respectively. When all bromine and iodine have been expelled, add silver nitrate. There should not be more than a slight opalescence, showing the absence of more than traces of chloride.

Bromate and Iodate.—To the dry salt, add dilute sulphuric acid, and allow to stand. There should be no brown coloration.

Iodide.—To the aqueous solution, add a few drops of very dilute, freshly prepared chlorine water, followed by starch mucilage. There should be no blue colour.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—(1) It should not lose more than 1 per cent of its weight when dried at 100°.

(2) The salt is estimated volumetrically by precipitation with standard silver nitrate.[1] Weigh about 1 gramme of the dried salt, dissolve, and dilute to 100 mils. Titrate portions of 20 mils with N/10 silver nitrate solution, using a few drops of potassium chromate solution as indicator. The silver nitrate reacts with the potassium bromide to produce a pale yellow precipitate of silver bromide. The precipitation is shown to be complete by the formation of a permanent reddish-brown precipitate of silver chromate, because

[1] It should be noted that the presence of any quantity of potassium chloride will result in a high titration value.

silver bromide is less soluble than silver chromate, and is, consequently, precipitated first:

$$AgNO_3 + KBr = AgBr + KNO_3,$$
$$170 \equiv 119,$$
$$1000 \text{ mils N/1 } AgNO_3 \equiv 119 \text{ grammes of KBr,}$$
$$1 \text{ mil N/10 } AgNO_3 \equiv 0{\cdot}0119 \text{ gramme of KBr.}$$

POTASSII IODIDUM

Potassium Iodide, KI. (Mol. Wt. = 166)

This salt, when dried at 100°, is required to contain not less than 99 per cent of KI.

Preparation.—It is manufactured by methods exactly similar to those employed for potassium bromide (*q.v.*), using iodine instead of bromine.

Properties.—Colourless, cubical crystals, opaque or transparent, with a saline taste. Soluble in less than 1 of water, and 1-12 in alcohol (90 per cent). The aqueous solution should be neutral, but may be slightly alkaline to litmus. The salt melts at a low red heat.

Tests for Impurities (to be applied to the aqueous solution). *Copper and Iron.*—Test as under Potassii Bromidum.

Aluminium.—Add excess of sodium hydroxide, filter if necessary, add to the filtrate ammonium chloride in excess, and boil. There should be no precipitate.

Calcium and Magnesium.—Test as under Potassii Bromidum.

Carbonate.—There should be no effervescence with dilute acids.

Sulphate.—Strongly acidify with hydrochloric acid, and add barium chloride, when there should not be more than a slight turbidity.

Chloride.—Add excess of dilute nitric acid, boil until colourless, then add silver nitrate. There should be no white precipitate.

Bromide and Nitrate.—Acidify with dilute sulphuric acid, and boil until any bromine and iodine (evolved owing to oxidation of some of the iodide by any bromate or iodate present) has been driven off. Divide the solution into two parts, and test as follows:

(1) Add sodium nitrite solution; boil until colourless; cool, and add a crystal of potassium iodate. There should not be more than the faintest brown colour, showing the absence of more than traces of bromide.

(2) To the second portion, add zinc and starch mucilage, when there should be no blue colour, showing absence of nitrate.

Bromate and Iodate.—To the dry salt, add dilute sulphuric acid, and allow to stand. There should be not more than the palest yellow coloration.

Cyanide.—Add dilute sulphuric acid and set aside in a closed tube for several minutes in order to decompose any bromate or

iodate. Invert the tube once or twice, then add excess of silver nitrate and filter off the precipitate, which will consist of silver iodide, with any bromide, chloride, or cyanide. Wash the precipitate thoroughly with boiling water, until a few drops of the filtrate, tested with dilute hydrochloric acid, give no opalescence. Boil the precipitate with moderately concentrated nitric acid, to decompose any silver cyanide, dilute, filter, and test the filtrate with dilute hydrochloric acid, when there should be no white precipitate or opalescence, showing absence of cyanide.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—(1) When dried at 100°, it should lose not more than 1 per cent of its weight.

(2) Potassium iodide is estimated by precipitation with standard silver nitrate in a manner similar to that described for Potassii Bromidum, weighing about 1·5 grammes of the dried salt, and using the same indicator.

$$AgNO_3 + KI = AgI + KNO_3,$$
$$170 = 166,$$
$$1000 \text{ mils N/1 } AgNO_3 \equiv 166 \text{ grammes of KI},$$
$$1 \text{ mil N/10 } AgNO_3 \equiv 0{\cdot}0166 \text{ gramme of KI}.$$

POTASSII CHLORAS

Potassium Chlorate, $KClO_3$. (Mol. Wt. = 122·5)

Preparation.—(1) It is formed when chlorine is passed into a hot, moderately concentrated solution of potassium hydroxide:

$$3Cl_2 + 6KOH = KClO_3 + 5KCl + 3H_2O.$$

The potassium chlorate, being much less soluble in cold water than potassium chloride, may be freed from the latter by fractional crystallisation.

(2) Commercially, this salt is produced by, first, passing chlorine into a boiling suspension of calcium hydroxide in water:

$$6Cl_2 + 6Ca(OH)_2 = Ca(ClO_3)_2 + 5CaCl_2 + 6H_2O,$$

and then adding potassium chloride to the hot solution, when double decomposition occurs:

$$Ca(ClO_3)_2 + 2KCl = CaCl_2 + 2KClO_3.$$

On concentrating and cooling, the potassium chlorate separates out, the much more soluble calcium chloride remaining in solution.

(3) Potassium chlorate is now prepared by the electrolysis of a solution of potassium chloride. The chlorine liberated at the anode is made to react with the caustic potash produced at the cathode, instead of being allowed to escape, as in the preparation of potassium hydroxide (p. 52).

Properties.—Colourless prisms or plates, with a saline taste. Soluble 1-16 in water. On heating it decrepitates, then melts and evolves oxygen :

$$2KClO_3 = KClO_4 + KCl + O_2,$$
$$KClO_4 = KCl + 2O_2.$$

Tests for Impurities (to be applied to the aqueous solution). *Iron.*—Acidify with dilute nitric acid and add potassium ferrocyanide, when there should be no blue or green colour.

Calcium and Magnesium.—Test as under Potassii Bromidum.

Sodium.—Apply the flame test.

Ammonium.—Boil with sodium hydroxide and test the evolved vapours with turmeric paper.

Nitrate.—Apply the brown ring test (p. 35).

Sulphate.—Acidify with hydrochloric acid and test with barium chloride, when there should not be more than a slight turbidity.

Chloride.—Acidify with nitric acid and add silver nitrate, when there should not be more than a slight opalescence.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

POTASSA SULPHURATA

Sulphurated Potash. *Syn.* Liver of Sulphur

This substance consists of a mixture of potassium trisulphide, K_2S_3, potassium pentasulphide, K_2S_5, and potassium thiosulphate, $K_2S_2O_3$, with smaller quantities of other potassium compounds. It is required to contain between 42 and 45 per cent of sulphur.

Preparation.—A mixture of dried potassium carbonate, 100 parts, and sublimed sulphur, 50 parts, is heated in a crucible (covered to exclude air), gently at first, and then to dull redness, until evolution of carbon dioxide ceases and the mass is fused. The fused mass is poured out on to a clean stone slab, allowed to cool, broken into fragments, and transferred to a stoppered bottle immediately.

$$3K_2CO_3 + 8S = 2K_2S_3 + K_2S_2O_3 + 3CO_2,$$
$$3K_2CO_3 + 12S = 2K_2S_5 + K_2S_2O_3 + 3CO_2.$$

Properties.—Granular fragments, the freshly fractured surface being pale liver-brown in colour, but rapidly changing to a greenish yellow on exposure to air. It has an acrid, alkaline taste, and a strong odour of hydrogen sulphide. It should be readily and almost completely soluble in water, with formation of a yellowish, opalescent solution. On treatment with dilute acids it is decomposed with rapid evolution of hydrogen sulphide.

Quantitative Estimation.—The sulphur present is estimated by oxidising to sulphate, precipitating as barium sulphate, and weighing. Dissolve about 0·2 gramme in about 10 mils of water in a

small flask. Add 5 mils of 1-5 solution of sodium hydroxide, heat to boiling, and add gradually a slight excess of bromine, with frequent agitation. Acidify with hydrochloric acid, boil off the excess of bromine, add excess of barium chloride, collect the precipitate on a filter paper, wash, dry, ignite, and weigh.

$$BaCl_2 + Na_2SO_4 = BaSO_4 + 2NaCl,$$
$$BaSO_4 \equiv S,$$
$$233 \text{ grammes } BaSO_4 \equiv 32 \text{ grammes of S.}$$

POTASSII SULPHAS

Potassium Sulphate, K_2SO_4. (Mol. Wt. = 174)

This salt is required to contain not less than 99 per cent of K_2SO_4.

Preparation.—(1) It occurs in the Stassfurt deposits in the form of mineral *kainite*, $K_2SO_4,MgSO_4,MgCl_2,6H_2O$, from which it can be obtained by, first, extracting the magnesium chloride with a little water, then dissolving the residue in water and treating with potassium chloride :

$$K_2SO_4, MgSO_4 + 3KCl = 2K_2SO_4 + KCl,MgCl_2.$$

On evaporating and cooling, the less soluble potassium sulphate crystallises out.

(2) It is also obtained as a by-product of many manufacturing processes, as a result of the action of sulphuric acid on potassium salts.

Properties.—It forms colourless, rhombic crystals containing no water of crystallisation, and has a saline taste. Soluble 1-10 in water, the solution being neutral ; insoluble in alcohol (90 per cent). When heated, it first decrepitates and then melts.

Tests for Impurities (to be applied to the aqueous solution). *Copper.*—Add excess of ammonium hydroxide and filter. The filtrate should have no blue tinge and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—Acidify with nitric acid and test with potassium ferrocyanide, when there should be no blue or green colour.

Calcium and Magnesium.—Test as under Potassii Bromidum.

Sodium and Ammonium.—Test as under Potassii Chloras.

Nitrate.—Apply the brown ring test (p. 35).

Chloride.—Add nitric acid and silver nitrate, when there should not be more than a slight opalescence.

Acid Potassium Sulphate.—The aqueous solution should be neutral to litmus.

Lead Limit.—20 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

POTASSII NITRAS

Potassium Nitrate, KNO_3. (Mol. Wt. = 101.)
Syn. Purified Nitre. *Unofficial Syn.* Saltpetre

Preparation.—This salt is obtained from Chili saltpetre, $NaNO_3$, by adding potassium chloride to the hot, concentrated aqueous solution, and boiling:

$$NaNO_3 + KCl = KNO_3 + NaCl.$$

As sodium chloride is not very soluble in hot water, the bulk of it is precipitated and removed by canvas filters. The mother liquor is then set aside in tanks for the potassium nitrate to crystallise out, the formation of small crystals being induced by stirring.

Properties.—Colourless, four or six-sided, rhombic prisms, or a white crystalline powder, with a cooling, saline taste. Soluble 1·4 in water. On heating it melts and decomposes, with evolution of oxygen:

$$2KNO_3 = 2KNO_2 + O_2.$$

Tests for Impurities (to be applied to the aqueous solution). *Copper.*—Add excess of ammonium hydroxide and filter. The filtrate should have no blue tinge and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—Add nitric acid and test with potassium ferrocyanide, when there should be no blue or green colour.

Aluminium.—Add nitric acid and test as under Potassii Carbonas.

Zinc.—Add ammonium hydroxide and pass hydrogen sulphide through the solution, when there should be no precipitate.

Calcium and Magnesium.—Test as under Potassii Bromidum.

Sodium.—Apply the flame test.

Ammonium.—Add sodium hydroxide, and boil. Test the evolved vapours with turmeric paper (p. 32).

Sulphate.—Acidify with hydrochloric acid and test with barium chloride. There should be no turbidity.

Chloride and Iodide.—Add a slight excess of silver nitrate. If a precipitate be formed, add a few drops of ammonium hydroxide, shake, and filter. A pale yellow residue shows the presence of iodide. Acidify the filtrate with nitric acid, when a white precipitate will be formed if chloride be present.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

POTASSII BICHROMAS

Potassium Bichromate, $K_2Cr_2O_7$. (Mol. Wt. = 294.)
Syn. Potassium Dichromate

This salt is required to contain not less than 99 per cent of $K_2Cr_2O_7$.

Preparation.—Potassium dichromate is manufactured from chrome iron ore, Cr_2O_3,FeO. The ore is strongly heated with a mixture of potassium carbonate and lime in an open furnace:

$$4Cr_2O_3,FeO + 6K_2CO_3 + 2CaO + 7O_2 = 2CaCrO_4 + 6K_2CrO_4 + 2Fe_2O_3 + 6CO_2.$$

The product is cooled and extracted with boiling water, potassium sulphate then being added to the liquor to convert the calcium chromate into potassium chromate:

$$CaCrO_4 + K_2SO_4 = CaSO_4 + K_2CrO_4.$$

The hot liquid is next filtered from the precipitated calcium sulphate and treated with the theoretical quantity of sulphuric acid, to convert the potassium chromate into dichromate:

$$2K_2CrO_4 + H_2SO_4 = K_2Cr_2O_7 + K_2SO_4 + H_2O.$$

On cooling, the potassium dichromate crystallises out, and may be purified by recrystallisation from water.

Properties.—Large, orange-red, anhydrous crystals. Soluble 1-10 in water, forming an acid solution. It is a powerful oxidising agent, each molecule providing 3 atoms of oxygen available for oxidising purposes:

$$K_2Cr_2O_7 \longrightarrow K_2O + Cr_2O_3 + 3O.$$

Quantitative Estimation.—The estimation depends upon the oxidation of potassium iodide by the dichromate, with the liberation of the equivalent amount of iodine, the iodine being determined by titration with sodium thiosulphate solution. Weigh about 0·5 gramme, dissolve, and dilute to 100 mils. Take 20 mils of the solution for each titration; add a few drops of dilute sulphuric acid and about 2 grammes of potassium iodide. Titrate with N/10 thiosulphate solution, using starch mucilage as indicator:

$$K_2Cr_2O_7 + 7H_2SO_4 + 6KI = 4K_2SO_4 + Cr_2(SO_4)_3 + 3I_2 + 7H_2O,$$
$$2Na_2S_2O_3 + I_2 = 2NaI + Na_2S_4O_6,$$
$$Na_2S_2O_3,5H_2O \equiv I \equiv \frac{K_2Cr_2O_7}{6},$$
$$248 \text{ grammes} \equiv 49 \text{ grammes } K_2Cr_2O_7,$$
$$1000 \text{ mils N/1 } Na_2S_2O_3,5H_2O \equiv 49 \text{ grammes } K_2Cr_2O_7,$$
$$1 \text{ mil N/10 } Na_2S_2O_3,5H_2O \equiv 0·0049 \text{ gramme } K_2Cr_2O_7.$$

POTASSII PERMANGANAS

Potassium Permanganate, $KMnO_4$. (Mol. Wt. = 158)

This salt is required to contain not less than 99 per cent of $KMnO_4$.

Preparation.—Manganese dioxide is fused with a mixture of potassium hydroxide and potassium chlorate, the chlorate supplying the necessary oxygen:

$$MnO_2 + 2KOH + O = K_2MnO_4 + H_2O.$$

The green mass of potassium manganate is extracted with water and treated with carbon dioxide, in order to convert it into permanganate:

$$3K_2MnO_4 + 2CO_2 = 2KMnO_4 + MnO_2 + 2K_2CO_3.$$

The solution is then filtered and evaporated, when the permanganate separates in crystals.

Properties.—Slender, dark purple prisms, having a metallic lustre by reflected light. Soluble 1-20 in water, the solution being neutral. On heating, it decomposes with evolution of oxygen:

$$2KMnO_4 = K_2MnO_4 + MnO_2 + O_2.$$

Potassium permanganate is a powerful oxidising agent in acid, alkaline, or neutral solution. In acid solution, two molecules of permanganate can supply 5 atoms of oxygen available for oxidising purposes:

$$2KMnO_4 \longrightarrow K_2O + 2MnO + 5O.$$

Tests for Impurities. *Lead.*—Boil a little of the permanganate with concentrated hydrochloric acid until the colour has disappeared, dilute largely, and pass hydrogen sulphide through the liquid, when there should be no black precipitate or brown colour.

Arsenic.—Apply Fleitmann's test (p. 143).

Iron.—Boil with concentrated hydrochloric acid until colourless, dilute and test with potassium ferrocyanide, when there should be no blue or green colour.

Sodium.—Apply the flame test.

Ammonium.—Boil with sodium hydroxide, and test the evolved vapours with turmeric paper (p. 32).

Sulphate.—Boil with concentrated hydrochloric acid until colourless, dilute, and add barium chloride. There should be no precipitate.

Chloride.—Dissolve in water, acidify with dilute sulphuric acid, pass sulphur dioxide until colourless, then add silver nitrate, when there should be no precipitate.

Nitrate.—Dissolve in water, acidify with dilute sulphuric acid, add excess of ferrous sulphate, and warm until colourless. Cool, and apply the brown ring test (p. 35).

Quantitative Estimation.—Potassium permanganate is estimated by determining the amount of oxalic acid it is capable of oxidising. Weigh about 1 gramme, dissolve, and dilute to 250 mils. Take 20 mils for each titration, acidify with dilute sulphuric acid, heat to boiling, and titrate with N/10 oxalic acid until the solution is colourless:

$$5(COOH)_2 + 2KMnO_4 + 3H_2SO_4 = K_2SO_4 + 2MnSO_4 + 10CO_2 + 8H_2O,$$
$$5(COOH)_2,2H_2O \equiv 2KMnO_4,$$
$$5 \times 126 \equiv 316,$$
$$1000 \text{ mils N/1 } (COOH)_2,2H_2O \equiv 31{\cdot}6 \text{ grammes } KMnO_4,$$
$$1 \text{ mil N/10 } (COOH)_2,2H_2O \equiv 0{\cdot}00316 \text{ gramme } KMnO_4.$$

Liquor Potassii Permanganatis. *Solution of Potassium Permanganate.*—This is a simple 1 per cent *w/v* solution of the salt in water. It may be tested for strength by titrating portions of 10 mils with N/10 oxalic acid, as described above.

POTASSII ACETAS

Potassium Acetate, $CH_3 . COOK$. (Mol. Wt. = 98)

This salt is required to contain not less than 90 per cent of $CH_3 . COOK$.

Preparation.—It may be prepared by dissolving potassium carbonate in a very slight excess of acetic acid, and gently evaporating to dryness in a porcelain dish on a sand-bath :

$$K_2CO_3 + 2CH_3 . COOH = 2CH_3 . COOK + CO_2 + H_2O.$$

Owing to the impurities that the carbonate is liable to contain, a purer sample of acetate may be obtained by using the bicarbonate.

Properties.—Satin-like crystalline masses, or a white, granular powder, having a saline taste. Very deliquescent. Soluble 1-0·5 in water, 1-2 in alcohol (90 per cent). The aqueous solution is alkaline to litmus owing to partial hydrolysis.

Tests for Impurities. *Copper, Iron, Aluminium, Calcium, and Magnesium.*—There should be no indication of any of these on testing as described under Potassii Carbonas.

Carbonate.—There should be no effervescence with dilute acids.

Sulphide.—Acidify the dry salt with hydrochloric acid and warm gently, when the evolved vapours should not blacken lead acetate paper.

Sulphate.—Acidify the aqueous solution with hydrochloric acid and add barium chloride, when there should be not more than a faint turbidity.

Chloride.—Dissolve in dilute nitric acid and test with silver nitrate, when there should not be more than a slight opalescence.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—This is based on the titration of the alkaline residue obtained by igniting the salt. Weigh about 1 gramme in a porcelain crucible and heat, very gently at first (in order to avoid loss by spurting), and finally to bright redness. Allow the crucible and contents to cool, boil in a dish with a little water and carefully filter. Rinse the crucible and dish repeatedly with small quantities of water, and pass the washings through the filter. Dilute the combined filtrate and washings to 100 mils, and titrate 20 mils at a time with N/10 sulphuric acid, using methyl orange as indicator :

$$2CH_3 . COOK \xrightarrow{} K_2CO_3,$$
$$K_2CO_3 + H_2SO_4 = K_2SO_4 + H_2O + CO_2,$$
$$H_2SO_4 \equiv 2CH_3 . COOK,$$
$$98 \equiv 2 \times 98,$$
$$1000 \text{ mils N/1 } H_2SO_4 \equiv 98 \text{ grammes } CH_3 . COOK,$$
$$1 \text{ mil N/10 } H_2SO_4 \equiv 0{\cdot}0098 \text{ gramme } CH_3 . COOK.$$

POTASSII TARTRAS

Potassium Tartrate $(K_2C_4H_4O_6)_2,H_2O$. (Mol. Wt. = 470)

This is required to contain not less than 99 per cent of $(K_2C_4H_4O_6)_2,H_2O$.

Preparation.—It is prepared by neutralising a solution of acid potassium tartrate with potassium carbonate, and crystallising:

$$2KHC_4H_4O_6 + K_2CO_3 = 2K_2C_4H_4O_6 + H_2O + CO_2.$$

Properties.—Small colourless prisms with a saline taste. Soluble 1·1 in water, forming a neutral solution. As may be seen from the formula given above, two molecules crystallise with one molecule of water.

Tests for Impurities.—Ignite the salt, digest the charred residue with dilute hydrochloric acid, filter, and apply the tests for the metallic impurities to the filtrate.

Copper and Iron.—There should be no indications of these, when tested as under Potassii Carbonas.

Calcium, Magnesium, and Sodium.—Only very slight reactions should be given when tested as under Potassii Carbonas.

Chloride and Sulphate.—Apply the tests described under Potassii Carbonas to an aqueous solution of the salt. Not more than very slight reactions should be given.

Acid Potassium Tartrate.—The aqueous solution of the salt should be neutral to litmus.

Lead Limit.—20 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—Potassium tartrate is estimated in a similar manner to that described under Potassii Acetas, the same quantities being employed:

$$(K_2C_4H_4O_6)_2,H_2O \longrightarrow 2K_2CO_3,$$
$$K_2CO_3 + H_2SO_4 = K_2SO_4 + CO_2 + H_2O,$$
$$2H_2SO_4 \equiv (K_2C_4H_4O_6)_2,H_2O,$$
$$2 \times 98 \equiv 470,$$
$$1000 \text{ mils N/1 } H_2SO_4 \equiv 117{\cdot}5 \text{ grammes } (K_2C_4H_4O_6)_2,H_2O,$$
$$1 \text{ mil N/10 } H_2SO_4 \equiv 0{\cdot}01175 \text{ gramme } (K_2C_4H_4O_6)_2,H_2O.$$

POTASSII TARTRAS ACIDUS

Acid Potassium Tartrate, $KHC_4H_4O_6$. (Mol. Wt. = 188)
Syn Purified Cream of Tartar

This is required to contain not less than 99 per cent of $KHC_4H_4O_6$.

Preparation.—Argol or crude acid potassium tartrate is deposited during the fermentation of grape juice (p. 288). It is purified by recrystallisation from water.

Properties.—A white, somewhat gritty powder, or in irregular crystalline fragments, having an acid taste and reaction. Soluble 1-220 in water; insoluble in alcohol (90 per cent).

Tests for Impurities. *Copper, Iron, Calcium, Magnesium, Sodium, Chloride, and Sulphate.*—Test as described under Potassii Tartras.

Lead and Arsenic Limits.—As for Potassii Tartras.

Quantitative Estimation.—(1) This estimation is based upon the complete neutralisation of the acid salt with standard sodium hydroxide solution. Owing to the sparing solubility of the salt it is not practicable to make up a solution of known strength for titration in aliquot parts. Weigh about 0·5 gramme, dissolve in 40 mils of N/10 sodium hydroxide, and titrate the excess of alkali with N/10 sulphuric acid, using methyl orange as indicator. The volume of acid required, subtracted from the number of mils of alkali added, gives the number of mils of alkali used in neutralising the acid potassium tartrate:

$$NaOH + KHC_4H_4O_6 = NaKC_4H_4O_6 + H_2O,$$
$$40 = 188,$$
$$1000 \text{ mils N/1 NaOH} = 188 \text{ grammes of } KHC_4H_4O_6,$$
$$1 \text{ mil N/10 NaOH} = 0{\cdot}0188 \text{ gramme of } KHC_4H_4O_6.$$

(2) The salt may also be estimated by the ignition method, as described for Potassii Tartras:

$$2KHC_4H_4O_6 \longrightarrow K_2CO_3.$$

POTASSII CITRAS

Potassium Citrate, $K_3C_6H_5O_7,H_2O$. (Mol. Wt. = 324)

This is required to contain not less than 99 per cent of $K_3C_6H_5O_7,H_2O$.

Preparation.—This salt may be prepared by neutralising a solution of citric acid by the addition of potassium bicarbonate until effervescence ceases. The liquid is then filtered and evaporated to dryness:

$$3K_2CO_3 + 2H_3C_6H_5O_7 = 2K_3C_6H_5O_7 + 3H_2O + 3CO_2.$$

Properties.—A white, granular or crystalline powder, deliquescent on exposure to air. Soluble 1-1 in water, the aqueous solution being alkaline to litmus. On heating, it first loses water then turns brown,

and finally chars, inflammable gases with a pungent odour being evolved.

Tests for Impurities.—Ignite the salt to destroy organic matter, boil the residue with dilute hydrochloric acid, filter, and employ the filtrate for testing for metallic impurities.

Iron, Calcium, Magnesium, and Sodium.—Test as described under Potassii Carbonas. There should be no reaction for any of these impurities.

Carbonate.—There should be no effervescence on moistening the dry salt with dilute sulphuric acid.

Chloride and Sulphate.—There should not be more than the slightest indication of these on testing as under Potassii Carbonas.

Tartrate.—A solution of 1 gramme in 1 mil of water should not deposit any precipitate on the addition of 1 mil of acetic acid.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—The salt is estimated by titrating the alkaline residue left on ignition in precisely the same manner as described for Potassii Acetas, employing the same quantity:

$$2K_3C_6H_5O_7,H_2O \longrightarrow 3K_2CO_3,$$
$$H_2SO_4 + K_2CO_3 = K_2SO_4 + H_2O + CO_2,$$
$$3H_2SO_4 = 2K_3C_6H_5O_7,H_2O,$$
$$3 \times 98 = 2 \times 324,$$
$$1000 \text{ mils } N/1\ H_2SO_4 = 108 \text{ grammes of } K_3C_6H_5O_7,H_2O,$$
$$1 \text{ mil } N/10\ H_2SO_4 = 0{\cdot}0108 \text{ gramme of } K_3C_6H_5O_7,H_2O.$$

COMPOUNDS OF SODIUM

Na (Atomic Wt. = 23)

The compounds of sodium used in pharmacy are even more numerous than those of potassium, because sodium salts occur more abundantly in Nature than potassium salts, and, consequently, the natural salts and products prepared from them are relatively cheap. The therapeutic action and chemical properties of corresponding sodium and potassium compounds are usually similar, but, generally speaking, sodium salts are more soluble in water than potassium salts.

The chief naturally occurring compound of sodium is the chloride, NaCl, which is present in sea water and is found also in mineral deposits (p. 74). Large quantities of Chili saltpetre, $NaNO_3$, are obtained from deposits in South America.

General Test for Sodium.—Even minute quantities of sodium compounds impart a vivid yellow colour to the bunsen flame. Owing to the solubility of sodium compounds there is no convenient and reliable precipitant available, so that it is customary to depend upon the flame test to prove the presence of sodium, precipitable metals having been proved to be absent, or, if present, having been removed.

SODII CARBONAS

Sodium Carbonate, $Na_2CO_3,10H_2O$. *(Mol. Wt. = 286)*

This is required to contain not less than ·*99 per cent of* $Na_2CO_3,10H_2O$.

Preparation.—Sodium carbonate is prepared on the large scale by three common processes.

(1) *The Le Blanc Black Ash Process.*—Sodium chloride from natural sources is heated in iron pans with sulphuric acid, when sodium hydrogen sulphate and hydrochloric acid are formed :

$$NaCl + H_2SO_4 = NaHSO_4 + HCl.$$

On raising the temperature the sodium hydrogen sulphate reacts with more sodium chloride to produce sodium sulphate and more hydrochloric acid (p. 15) :

$$NaCl + NaHSO_4 = Na_2SO_4 + HCl.$$

The sodium sulphate is next mixed with limestone and coal in a revolving cylinder, through which the heat from a furnace is allowed to pass, the product being called " black-ash ". During the heating the sulphate is reduced by the carbon to sulphide :

$$Na_2SO_4 + 4C = Na_2S + 4CO,$$

and the sulphide reacts with the limestone to produce sodium carbonate and calcium sulphide :

$$Na_2S + CaCO_3 = Na_2CO_3 + CaS.$$

The black-ash is lixiviated with water, the solution of sodium carbonate decanted, and then evaporated in shallow pans. The product is purified by recrystallisation from water.

(2) *The Ammonia-soda or Solvay's Process.*—A cool, saturated solution of sodium chloride from the salt works is treated with ammonia and carbon dioxide, when ammonium bicarbonate is formed :

$$NH_3 + H_2O + CO_2 = NH_4HCO_3,$$

and this reacts with the sodium chloride to produce sodium bicarbonate :

$$NH_4HCO_3 + NaCl = NH_4Cl + NaHCO_3.$$

The sodium bicarbonate separates out on account of its being less soluble, and is removed from the mother liquor by filtration. On heating it evolves carbon dioxide (which may be used again) and leaves anhydrous sodium carbonate, from which the official substance may be obtained by crystallisation from water. The ammonium chloride formed during the process on heating with lime evolves ammonia, which may be employed again, so that calcium chloride is the only waste product. This process is thus much more economical than the Le Blanc process, and it is only on account of the hydro-

chloric acid produced as a by-product that the latter process holds its own.

(3) *Electrolytic Process.*—Sodium hydroxide, obtained by the electrolysis of aqueous solutions of sodium chloride (cf. p. 52), is treated with carbon dioxide. The chlorine evolved during the electrolysis is utilised in the preparation of bleaching powder (p. 10).

Properties. — It occurs in transparent, colourless, rhombic crystals, which become efflorescent through loss of water on exposure, the efflorescent salt containing only five molecules of water. Taste strongly alkaline. Soluble 1-2 in water, the solution being strongly alkaline to litmus. On heating it liquefies, dissolving in its own water of crystallisation; above 80° it loses all its water and dries, the loss amounting to 62·9 per cent of its weight. The anhydrous substance melts, without decomposition, at a dull red heat.

Twenty parts of sodium carbonate are neutralised by 9·8 parts of citric acid and 10·5 parts of tartaric acid.

Tests for Impurities. *Copper.*—Dissolve in dilute hydrochloric acid, add excess of ammonium hydroxide, and filter. The filtrate should have no blue tinge, and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—Dissolve in excess of nitric acid and add potassium ferrocyanide. There should be no blue or green colour.

Aluminium.—Dissolve in excess of dilute nitric acid, add excess of sodium hydroxide, filter off any precipitate of iron, then add to the filtrate excess of ammonium chloride, and boil. No white precipitate should be produced.

Calcium.—Dissolve in slight excess of dilute hydrochloric acid, make alkaline with ammonium hydroxide, and test with ammonium oxalate, when there should be no white precipitate.

Ammonium.—When warmed with sodium hydroxide solution not more than the slightest odour of ammonia should be detectable.

Sulphate.—A solution in hydrochloric acid should yield not more than a slight turbidity with barium chloride.

Sulphite and Thiosulphate.—Dissolve in excess of dilute hydrochloric acid and add barium chloride. Filter off from any precipitate of sulphate and add bromine water to the filtrate, when there should be no precipitate (cf. p. 30). The aqueous solution should yield no precipitate of sulphur on acidification with hydrochloric acid.

Chloride.—Dissolve in excess of dilute nitric acid, and test with silver nitrate, when there should not be more than a faint opalescence.

Thiocyanate.—Acidify the aqueous solution with hydrochloric acid, and add a few drops of very dilute ferric chloride solution. There should be no red coloration.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—The carbonate is estimated by neutralisation with standard sulphuric acid. Weigh about 10 grammes, dissolve, and dilute to 100 mils. Titrate portions of 20 mils with N/1 sulphuric acid, using methyl orange as indicator.

$$H_2SO_4 + Na_2CO_3,10H_2O = Na_2SO_4 + 11H_2O + CO_2,$$
$$98 \equiv 286,$$
$$1000 \text{ mils N/1 } H_2SO_4 \equiv 143 \text{ grammes of } Na_2CO_3,10H_2O,$$
$$1 \text{ mil N/1 } H_2SO_4 \equiv 0{\cdot}143 \text{ gramme of } Na_2CO_3,10H_2O.$$

SODII CARBONAS EXSICCATUS

Exsiccated Sodium Carbonate, Na_2CO_3. (Mol. Wt. = 106)

This is required to contain not less than 95 per cent of anhydrous sodium carbonate, Na_2CO_3.

Preparation.—It may be prepared by heating crystalline sodium carbonate until it has lost nearly 63 per cent of its weight.

Properties.—A whitish powder, with a strongly alkaline taste, freely, but somewhat slowly, soluble in water. It has a tendency to absorb moisture from the atmosphere and become converted into mono-hydrated sodium carbonate, for which reason it should be kept excluded from the air as far as possible. 53 parts are equivalent to about 142 parts of the crystalline carbonate.

It is inadvisable to use either this salt or the crystalline carbonate for analytical purposes, since both usually contain traces of chloride and sulphate. When the analytically pure substance is required it is most conveniently obtained by heating the purest form of sodium bicarbonate.

Tests for Impurities.—Test as described under Sodii Carbonas.

Lead Limit.—25 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—It is estimated in a manner similar to Sodii Carbonas. Weigh about 5 grammes, dissolve, dilute to 100 mils, and titrate portions of 20 mils with N/1 sulphuric acid, using methyl orange as indicator :

$$H_2SO_4 + Na_2CO_3 = Na_2SO_4 + H_2O + CO_2,$$
$$98 \equiv 106,$$
$$1000 \text{ mils N/1 } H_2SO_4 \equiv 53 \text{ grammes of } Na_2CO_3,$$
$$1 \text{ mil N/1 } H_2SO_4 \equiv 0{\cdot}053 \text{ gramme of } Na_2CO_3.$$

SODII BICARBONAS

Sodium Bicarbonate, $NaHCO_3$. (Mol. Wt. = 84)

This is required to contain not less than 98·5 per cent of $NaHCO_3$.

Preparation.—(1) Sodium bicarbonate (sodium hydrogen carbonate) is prepared by the ammonia-soda process as described under

Sodii Carbonas, but the product so obtained is liable to contain traces of ammonia.

(2) A purer form may be obtained by treating sodium carbonate, which has been obtained by the ammonia-soda process, with carbon dioxide. The crystallised sodium carbonate is placed in chambers having false bottoms through which the released water of crystallisation can escape :

$$Na_2CO_3, 10H_2O + CO_2 = 2NaHCO_3 + 9H_2O.$$

The bicarbonate is then purified by washing with small quantities of water or dilute alcohol to remove normal carbonate, chloride, and sulphate, the loss of bicarbonate being but small on account of its being less soluble.

Properties.—A white powder, or small opaque crystals, with a taste that is saline, but not disagreeably alkaline. Soluble 1-11 in water. The aqueous solution is faintly alkaline to litmus paper; on heating loses carbon dioxide, and when subsequently cooled deposits crystals of sodium sesquicarbonate, $Na_2CO_3,2NaHCO_3,2H_2O$; on boiling more carbon dioxide is lost, and the dissolved salt becomes converted into the normal carbonate.

Tests for Impurities. *Copper, Iron, Aluminium, Calcium, Ammonium, Sulphate, Sulphite, Thiosulphate, Chloride, and Thiocyanate.*—Test as described under Sodii Carbonas.

Limit of Normal Carbonate.—A solution of 1 gramme in 20 mils of water, obtained without shaking and at a temperature not exceeding 15°, should not at once assume a red colour on the addition of 2 drops of phenolphthalein; but if a red colour does appear, it should be discharged on the addition of 0·2 mil of N/1 H_2SO_4.

Lead Limit.—5 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—Sodium bicarbonate is estimated by neutralisation with standard sulphuric acid. Weigh about 5 grammes, dissolve in cold water, and dilute to 100 mils. Titrate portions of 20 mils with N/1 sulphuric acid, using methyl orange as indicator :

$$H_2SO_4 + 2NaHCO_3 = Na_2SO_4 + H_2O + CO_2.$$
$$98 = 2 \times 84,$$
$$1000 \text{ mils } N/1\ H_2SO_4 = 84 \text{ grammes of } NaHCO_3,$$
$$1 \text{ mil } N/1\ H_2SO_4 = 0{\cdot}084 \text{ gramme of } NaHCO_3.$$

Sodium Carbonate and Bicarbonate.—The proportion of these compounds present in a mixture may be determined as described under Potassii Bicarbonas (p. 57).

Sodium Carbonate and Hydroxide.—This mixture is commonly met with in the form of *soda-ash*, and the proportions of the two constituents may be estimated as described under Potassa Caustica (p. 53).

SODII CHLORIDUM

Sodium Chloride, NaCl. (Mol. Wt. = 58·5)

Preparation.—In some countries, commercial " salt " is obtained by evaporation of sea water, but in Britain it is mined in the form of rock-salt from deposits in Worcestershire and Cheshire. The rock-salt may be brought to the surface in blocks, or, more usually, water is introduced into a specially sunk well, and the resulting brine pumped up and evaporated in shallow pans. If calcium sulphate be present in any quantity, it separates first and is removed by means of perforated shovels. On further concentration the sodium chloride separates out, leaving more soluble potassium and magnesium salts in solution. The size of the crystals obtained depends upon the rate of evaporation of the solution—the quicker the rate the smaller the crystals.

Very pure sodium chloride, for analytical purposes, may be obtained by passing hydrogen chloride gas into a strong aqueous solution of the salt. Sodium chloride, being only slightly soluble in hydrochloric acid solution, crystallises out, leaving the impurities in solution.

Properties.—Small, colourless, cubical crystals, containing no water of crystallisation. Taste, saline. Soluble 1-3 in water, the solubility increasing but little with rise of temperature : for which reason it cannot be purified by recrystallisation from water. On heating, it first decrepitates, and then melts.

Tests for Impurities. *Iron* (*Limit of*).—20 mils of a 1-20 aqueous solution should not immediately be coloured blue by the addition of 0·5 mil of 5 per cent potassium ferrocyanide solution.

Calcium.—To the aqueous solution add ammonium oxalate. There should not be more than a slight turbidity.

Magnesium.—Addition of ammonium hydroxide to the aqueous solution, followed by sodium phosphate, should produce no immediate precipitate.

Potassium.—No crimson colour should be visible through an indigo prism on applying the flame test.

Sulphate.—Addition of barium chloride to the aqueous solution should produce not more than a slight turbidity.

Iodide.—To the aqueous solution add a few drops of dilute sulphuric acid, a little sodium nitrite, and starch mucilage. There should be no blue colour.

Bromide.—If iodide has been found it must be removed by boiling with dilute sulphuric acid and successive quantities of sodium nitrite until all the iodine has been expelled. Cool well, then add dilute nitric acid and a little potassium iodate, when, if bromide be present, a brown coloration due to liberated bromine and iodine will be formed on standing.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—There is no official volumetric test, but the salt may be estimated by titration with silver nitrate as described under Potassii Bromidum, using potassium chromate as indicator.

SODII BROMIDUM

Sodium Bromide, NaBr. (Mol. Wt. = 103)

This is required to contain not less than 99 per cent of NaBr when dried at 110°.

Preparation.—It may be prepared by a method analogous to that described under Potassii Bromidum, using sodium carbonate in place of potassium carbonate. In order to obtain the salt in the anhydrous form the solution must be crystallised at a temperature above 50°.

Properties.—Small, white, cubical, hygroscopic crystals, with a saline, somewhat bitter taste. Soluble 1·1·5 in water and 1·16 in alcohol (90 per cent). It melts without decomposition at a dull red heat.

Tests for Impurities. (To be applied to the aqueous solution.) *Copper, Iron, and Aluminium.*—Test as described under Sodii Carbonas.

Zinc.—Add ammonium chloride and ammonium hydroxide, then pass hydrogen sulphide, when there should be no precipitate.

Calcium.—Test as under Sodii Carbonas.

Magnesium.—Make alkaline with ammonium hydroxide and add sodium phosphate. There should be no precipitate.

Potassium.—Apply the flame test to the dry salt, using an indigo prism.

Ammonium.—Boil with sodium hydroxide and test the evolved vapours with turmeric paper (p. 32).

Carbonate, Sulphate, Chloride, Iodide, Bromate, and Iodate.—Test as described under Potassii Bromidum.

Cyanide.—Test as described under Potassii Iodidum.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—(1) It should not lose more than 5 per cent of its weight when dried at 110°.

[1] (2) The dried salt is estimated by precipitation with standard silver nitrate solution in precisely the same manner as Potassii Bromidum, using the same quantities:

$$AgNO_3 + NaBr = AgBr + NaNO_3,$$
$$170 \equiv 103,$$
$$1000 \text{ mils } N/1\ AgNO_3 \equiv 103 \text{ grammes of } NaBr,$$
$$1 \text{ mil } N/10\ AgNO_3 \equiv 0{\cdot}0103 \text{ gramme of } NaBr.$$

[1] See footnote, p. 58.

SODII IODIDUM

Sodium Iodide, NaI. (Mol. Wt. = 150)

This is required to contain not less than 99 per cent of NaI when dried at 110°.

Preparation.—It is prepared by methods similar to those employed in making potassium bromide (*q.v.*), using sodium carbonate in place of potassium carbonate and iodine instead of bromine. The salt should be crystallised above 20°.

Properties.—Colourless, cubical crystals or a white, deliquescent, crystalline powder, with a saline, somewhat bitter taste. Soluble about 2·1 in water and 1·3 in alcohol (90 per cent).

Tests for Impurities. (To be applied to the aqueous solution.) *Copper, Iron, and Aluminium.*—Test as described under Sodii Carbonas.

Calcium.—Test as under Sodii Carbonas.

Magnesium, Potassium, and Ammonium.—Test as described under Sodii Bromidum.

Carbonate, Sulphate, Bromate, Iodate, Bromide, Chloride, and Cyanide.—Test as described under Potassii Iodidum.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—(1) It should lose not more than 5 per cent of its weight when dried at 110°. (2) The dried salt is estimated by precipitation with standard silver nitrate solution in an exactly similar manner to that described under Potassii Bromidum, using potassium chromate as indicator:

$$AgNO_3 + NaI = AgI + NaNO_3,$$
$$170 \quad = 150,$$
$$1000 \text{ mils } N/1\ AgNO_3 = 150 \text{ grammes of NaI},$$
$$1 \text{ mil } N/10\ AgNO_3 = 0{\cdot}0150 \text{ gramme of NaI}.$$

SODII SULPHAS

Sodium Sulphate, $Na_2SO_4,10H_2O$. (Mol. Wt. = 322)

Syn. Glauber's Salt

Preparation.—Crude sodium sulphate (salt-cake) is obtained by the action of concentrated sulphuric acid on sodium chloride in the first stage of the Le Blanc process for the preparation of sodium carbonate (p. 70). The pure hydrated salt is prepared from the salt-cake by recrystallisation from water.

Properties.—Transparent, efflorescent prisms, with a saline, bitter taste. Soluble 1·3 in water at 15°. With rise of temperature the solubility increases to a maximum of 1·0·3 at 33°, and then decreases. On boiling a strong solution, crystals of anhydrous sodium sulphate are deposited. Insoluble in alcohol.

Tests for Impurities. (To be applied to the aqueous solution.) *Iron.*—Add nitric acid and potassium ferrocyanide, when there should be no blue or green colour.

Magnesium and Potassium.—There should be no indication of these when tested as under Sodii Chloridum.

Ammonium.—Boil with ammonium hydroxide and test the evolved vapours with turmeric paper (p. 32)

Carbonate.—There should be no precipitate on the addition of magnesium sulphate solution, in the cold or on boiling. The dry salt should not effervesce with dilute acids.

Chloride.—Acidify with nitric acid and add silver nitrate, when there should not be more than a faint opalescence.

Lead Limit.—5 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—(1) When heated the salt melts at 33° and loses all its water of crystallisation at 100°, the loss in weight being 55·9 per cent.

(2) The sulphate in the salt is estimated by precipitation as barium sulphate, the precipitate being collected, dried, and weighed.

Weigh out about 0·5 to 1 gramme of the salt, and dissolve in about 200 mils of water in a large beaker. Add a few drops of dilute hydrochloric acid, heat to boiling, and add, drop by drop, a slight excess of hot dilute barium chloride solution. Allow to stand for fifteen minutes, and decant the supernatant liquid through a filter. Transfer every trace of the precipitate to the filter by repeatedly rinsing the beaker with water, adhering particles being loosened by means of a rubber-tipped glass rod, the same being used as a guiding rod for transferring the liquor to the filter. Finally wash the filter with warm water until the washings are free from chloride (tested with silver nitrate), and dry the filter-paper and contents in a water-oven.

Place the filter-paper and precipitate in a weighed crucible, and ignite, very gently at first, and then to redness, until all the carbon from the filter-paper has burned away. In order to reconvert any barium sulphide that may have been formed, by the reducing action of the carbon, into sulphate, add three or four drops of a mixture of concentrated sulphuric and nitric acids, and again ignite. Cool the crucible in a desiccator and weigh. Repeat the ignition, again cool and weigh, and continue this procedure until the weight is constant:

$$Na_2SO_4 + BaCl_2 = BaSO_4 + 2NaCl,$$
$$BaSO_4 = Na_2SO_4,10H_2O,$$
$$233 \text{ grammes of } BaSO_4 \equiv 322 \text{ grammes of } Na_2SO_4,10H_2O.$$

SODII NITRIS

Sodium Nitrite, $NaNO_2$. (Mol. Wt. = 69.)

This is required to contain not less than 95 per cent of $NaNO_2$.

Preparation.—Sodium nitrite can be made by strongly heating sodium nitrate :

$$2NaNO_3 = 2NaNO_2 + O_2.$$

In practice, however, the sodium nitrate is heated with metallic lead, which acts as a reducing agent :

$$NaNO_3 + Pb = NaNO_2 + PbO.$$

The mass is allowed to cool, extracted with water, filtered, and the filtrate concentrated to crystallisation.

Properties.—A white, deliquescent crystalline powder with a saline taste. The commercial substance is often met with in the form of sticks. Soluble 1-1·5 in water ; slightly soluble in alcohol. It is decomposed by dilute acids with evolution of pale brown fumes, owing to the instability of the liberated nitrous acid.

Tests for Impurities. *Free Alkali.*—The aqueous solution should be neutral, or only very slightly alkaline to litmus.

Lead.—A concentrated aqueous solution should give no precipitate of lead sulphate with dilute sulphuric acid.

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—The salt is oxidised to nitrate by standard potassium permanganate solution in presence of sulphuric acid. It is not permissible to acidify the nitrite and titrate with the permanganate, since the liberated nitrous acid would be decomposed with liberation of nitrogen peroxide before oxidation. The usual procedure, therefore, is to make a solution of the nitrite and run this from the burette into a known volume of warm standard potassium permanganate solution acidified with sulphuric acid. Weigh about 1 gramme of the nitrite, dissolve in cold water, and dilute to 250 mils. Fill a burette with this solution and slowly discharge into 20 mils of N/10 potassium permanganate, previously strongly acidified with dilute sulphuric acid and warmed to about 50°, until the colour disappears :

$$2NaNO_2 + H_2SO_4 = Na_2SO_4 + 2HNO_2,$$
$$2KMnO_4 + 5HNO_2 + 3H_2SO_4 = K_2SO_4 + 2MnSO_4 + 5HNO_3 + 3H_2O,$$
$$2KMnO_4 \equiv 5HNO_2 \equiv 5NaNO_2,$$
$$316 \equiv 345 \text{ grammes of } NaNO_2,$$
$$1000 \text{ mils N/1 } KMnO_4 \equiv 34{\cdot}5 \text{ grammes of } NaNO_2,$$
$$1 \text{ mil N/10 } KMnO_4 \equiv 0{\cdot}00345 \text{ gramme } NaNO_2.$$

SODII PHOSPHAS

Sodium Phosphate, $Na_2HPO_4,12H_2O$. (Mol. Wt. = 358)
Syn. Disodium hydrogen phosphate

This is required to contain 99·5 per cent of $Na_2HPO_4,12H_2O$.

Preparation.—(1) Disodium hydrogen phosphate can be made

by adding sodium carbonate to phosphoric acid solution until alkaline :

$$Na_2CO_3 + H_3PO_4 = Na_2HPO_4 + CO_2 + H_2O.$$

(2) It is manufactured from bone-ash by, first, treating with sulphuric acid, when calcium sulphate is precipitated and acid calcium phosphate (p. 40) passes into solution :

$$Ca_3(PO_4)_2 + 2H_2SO_4 = Ca(H_2PO_4)_2 + 2CaSO_4,$$

and then adding boiling water and filtering. The filtrate, on treatment with sodium carbonate, deposits dicalcium phosphate (p. 40), leaving disodium hydrogen phosphate in solution :

$$Ca(H_2PO_4)_2 + Na_2CO_3 = Na_2HPO_4 + CaHPO_4 + CO_2 + H_2O.$$

The dicalcium phosphate is filtered off, and the filtrate, on concentrating and cooling, deposits crystals of disodium hydrogen phosphate.

Properties. — Large colourless prisms, with a saline taste. Soluble 1·7 in water, the solution being very slightly alkaline to litmus. The crystals slowly effloresce in air, losing 5 molecules of water of crystallisation. On heating, the salt loses the whole of its water of crystallisation, and on igniting becomes converted into sodium pyrophosphate :

$$2Na_2HPO_4 = Na_4P_2O_7 + H_2O.$$

Tests for Impurities. *Potassium.*—Apply the flame test, using an indigo prism.

Ammonium.—Boil with sodium hydroxide, and test the evolved vapours with turmeric paper (p. 32).

Carbonate.—There should be no effervescence with dilute acids.

Sulphate.—A solution in hydrochloric acid should not give more than a slight turbidity with silver nitrate.

Chloride.—A nitric acid solution of the salt should yield no opalescence with silver nitrate.

Lead Limit.—5 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—This depends upon the fact that disodium hydrogen phosphate is alkaline to methyl orange, whereas sodium dihydrogen phosphate is neutral to this indicator (p. 42). Weigh about 5 grammes, dissolve, and dilute to 100 mils. Titrate portions of 20 mils with N/10 sulphuric acid, using methyl orange as indicator :

$$\underset{98}{H_2SO_4} + \underset{\equiv \quad 716,}{2Na_2HPO_4,12H_2O} = 2NaH_2PO_4 + Na_2SO_4 + 12H_2O,$$

$$1000 \text{ mils N/1 } H_2SO_4 \equiv 358 \text{ grammes of } Na_2HPO_4,12H_2O,$$
$$1 \text{ mil N/10 } H_2SO_4 \equiv 0{\cdot}0358 \text{ gramme of } Na_2HPO_4,12H_2O.$$

Sodii Phosphas Effervescens. *Effervescent Sodium Phosphate.*—This is prepared by mixing together previously dehydrated

sodium phosphate, sodium bicarbonate, tartaric acid, and citric acid, and heating the mixture on a water-bath until it has assumed a pasty consistency, when it is forced through a sieve of suitable mesh to produce granules of uniform size. The granules are then dried at a temperature not exceeding 55°. In the presence of a small quantity of water of crystallisation released from the citric acid a small proportion of the mixed acids reacts with a little of the bicarbonate with evolution of carbon dioxide, which assists granulation.

The total loss in weight is about one-seventh of the whole, so this must be allowed for in calculating the quantities necessary to produce a definite amount

SODII PHOSPHAS ACIDUS

Acid Sodium Phosphate, $NaH_2PO_4,2H_2O$. (Mol. Wt. = 156.)
Syns. Sodium dihydrogen phosphate; Sodium biphosphate

This is required to contain not less than 70 per cent of NaH_2PO_4, corresponding to about 91 per cent of the hydrated salt. The amount of water of crystallisation is somewhat variable.

Preparation.—Phosphoric acid is added to a hot solution of sodium carbonate until the solution is slightly acid to litmus, disodium hydrogen phosphate being formed. A further and equal quantity of phosphoric acid is then added to form the sodium dihydrogen salt:

$$H_3PO_4 + Na_2CO_3 = Na_2HPO_4 + H_2O + CO_2,$$
$$Na_2HPO_4 + H_3PO_4 = 2NaH_2PO_4.$$

The solution is then concentrated, cooled, and allowed to crystallise.

Properties.—Colourless, rhombic crystals, or in a crystalline powder, with a saline, acid taste. Soluble about 1·1 in water, the solution being acid to litmus. On heating to 100° the salt loses its water of crystallisation, at 250° it becomes converted into metaphosphate, and on strong ignition it yields pyrophosphate (p. 39).

Tests for Impurities. *Potassium and Ammonium.*—Test as under Sodii Phosphas.

Sulphate and Chloride.—There should not be more than the slightest indications of these on testing as under Sodii Phosphas.

Lead Limit.—5 parts per million (p. 172).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—It is estimated by conversion into the disodium salt by titration with alkali in presence of glycerin. The disodium hydrogen phosphate formed is slightly hydrolysed in aqueous solution, but the hydrolysis is prevented by the presence of the glycerin, a sharper end-point being obtained Weigh about 10 grammes, dissolve, and dilute to 100 mils. Titrate portions of

20 mils, mixed with an equal volume of glycerin, with N/1 sodium hydroxide, using phenolphthalein as indicator:

$$NaOH + NaH_2PO_4 = Na_2HPO_4 + H_2O,$$
$$40 \equiv 120,$$
$$1000 \text{ mils N/1 } NaOH \equiv 120 \text{ grammes of } Na_2HPO_4,$$
$$1 \text{ mil N/1 } NaOH \equiv 0{\cdot}120 \text{ gramme of } Na_2HPO_4.$$

SODII HYPOPHOSPHIS

Sodium Hypophosphite, NaH_2PO_2. (Mol. Wt. = 88)

This is required to contain not less than 97 per cent of NaH_2PO_2 when dried at 110°.

Preparation.—Sodium hypophosphite is the sodium salt of hypophosphorous acid, H_3PO_2, which is a monobasic acid although it contains three atoms of hydrogen. When phosphorus is heated with milk of lime, a spontaneously inflammable mixture of phosphine and other phosphides of hydrogen is evolved, and a solution of calcium hypophosphite is formed:

$$8P + 3Ca(OH)_2 + 6H_2O = 3Ca(H_2PO_2)_2 + 2PH_3.$$

On the addition of the theoretical quantity of sodium carbonate to the solution, calcium carbonate is precipitated and is removed by filtration; the filtrate, containing sodium hypophosphite, is then carefully evaporated to dryness on a water-bath:

$$Ca(H_2PO_2)_2 + Na_2CO_3 = 2NaH_2PO_2 + CaCO_3.$$

Properties.—White, deliquescent granules, with a bitter, nauseous taste. Soluble 1-1 in water, and 1-30 in alcohol (90 per cent); insoluble in ether. When heated, it evolves a spontaneously inflammable mixture of hydrogen, phosphine, and other phosphides of hydrogen:

$$5NaH_2PO_2 = Na_4P_2O_7 + NaPO_3 + 2PH_3 + 2H_2.$$

It is a powerful reducing agent, precipitating metallic gold, silver and mercury from solutions of their salts, and reducing sulphurous acid to sulphur. On warming with copper sulphate solution, a red precipitate of cuprous hydride is obtained, and on boiling, hydrogen is evolved and copper deposited:

$$3H_3PO_2 + 4CuSO_4 + 6H_2O = 3H_3PO_4 + 4H_2SO_4 + 2Cu_2H_2.$$

Tests for Impurities (to be applied to the aqueous solution). *Copper, Iron, and Aluminium.*—Test as described under Sodii Carbonas.

Zinc.—Add ammonium chloride, ammonium hydroxide, and ammonium sulphide. There should be no white precipitate.

Calcium.—Test as under Sodii Carbonas.

Magnesium.—There should be no precipitate with ammonium hydroxide and sodium phosphate, even on standing.

Potassium.—Apply the flame test, using an indigo prism.

Ammonium.—Boil with sodium hydroxide, and test the evolved vapours with turmeric paper.

Carbonate.—There should be no distinct effervescence with mineral acids.

Sulphate and Chloride.—Test as under Sodii Carbonas.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—(1) It should lose not more than 2 per cent of its weight when carefully dried at 110°.

(2) The salt is estimated by oxidation in acid solution with excess of standard potassium dichromate, the excess being determined by addition of potassium iodide, and titration of the liberated iodine with standard sodium thiosulphate solution:

$$\text{(i.)} \quad 2NaH_2PO_2 + H_2SO_4 = Na_2SO_4 + 2H_3PO_2.$$

$$\text{(ii.)} \quad 2K_2Cr_2O_7 + 3H_3PO_2 + 8H_2SO_4 = 2K_2SO_4 + 2Cr_2(SO_4)_3 + 3H_3PO_4 + 8H_2O.$$

As the salt may contain some phosphite, which is also a reducing agent, this must first be removed by precipitation as lead phosphite, the soluble lead hypophosphite remaining in solution. Weigh about 2·5 grammes of the dried salt, dissolve in about 50 mils of water, add about 5 mils of 10 per cent lead acetate solution, and dilute to 100 mils. Shake well, and filter through a double filter. To 20 mils of the filtrate add 40 mils of N/1 potassium dichromate, acidify with dilute sulphuric acid, heat on a water-bath for one hour, cool, and dilute to 250 mils. To 20 mils of this solution—corresponding to 0·04 gramme of the hypophosphite and 3·2 mils of N/1 or 32 mils of N/10 dichromate—add 2 grammes of potassium iodide, and then titrate the liberated iodine with N/10 sodium thiosulphate solution, using starch mucilage as indicator.

One volume of N/10 thiosulphate is equivalent to the iodine liberated by one volume of N/10 potassium dichromate; therefore, subtract the volume of N/10 thiosulphate required from 32 (*vide supra*), when the result will be the volume of N/10 dichromate equivalent to 0·04 gramme of the hypophosphite:

$$2K_2Cr_2O_7 \equiv 3NaH_2PO_2 \text{ (from equations (i.) and (ii.))},$$
$$2 \times 294 \equiv 3 \times 88,$$
$$1000 \text{ mils N/1 } K_2Cr_2O_7 \equiv \frac{88}{4} = 22 \text{ grammes } NaH_2PO_2,$$
$$1 \text{ mil N/10 } K_2Cr_2O_7 \equiv 0{\cdot}0022 \text{ gramme } NaH_2PO_2.$$

SODII ARSENAS ANHYDROSUS

Anhydrous Sodium Arsenate, Na_2HAsO_4. (Mol. Wt. = 186)

This is required to contain not less than 98 per cent of Na_2HAsO_4.

Preparation.—This salt is obtained by exsiccating crystalline sodium arsenate by heating to a temperature of 150°. The crystalline salt may be produced by finely powdering and mixing arsenious

oxide 10 parts, sodium nitrate 8·5 parts, and exsiccated sodium carbonate 5·5 parts. The mixture is transferred to a crucible, and heated to redness until gases are no longer evolved and it is completely fused. The liquid mass is poured out on to a slab and allowed to solidify; then, while still warm, it is mixed with 35 parts of boiling water, with constant stirring, the liquid filtered and set aside to crystallise. The crystals are drained, dried between filter paper on a porous plate and transferred to a stoppered bottle as quickly as possible. If the anhydrous salt is required the solution may be evaporated in a tared dish on a sand-bath and the residue heated at a temperature not exceeding 150° until the weight is constant.

The sodium nitrate oxidises the arsenious oxide to arsenic oxide, which then reacts with the sodium carbonate to produce sodium arsenate. By action of heat, however, this is converted into pyroarsenate, so that the reaction may be represented by the following equation:

$$As_2O_3 + Na_2CO_3 + 2NaNO_3 = Na_4As_2O_7 + CO_2 + N_2O_3.$$

When boiled with water, the pyroarsenate is converted into disodium hydrogen arsenate, thus:

$$Na_4As_2O_7 + H_2O = 2Na_2HAsO_4.$$

Properties.—A white powder, soluble 1-6 in water, the solution being alkaline to litmus; slightly soluble in alcohol (90 per cent). The addition of magnesium ammonio-sulphate solution (p. 40), or of nitric acid and ammonium molybdate solution to the aqueous solution of sodium arsenate, produces in the former case a white crystalline precipitate, and in the latter case a yellow precipitate, similar to those yielded by disodium hydrogen phosphate with these reagents, but silver nitrate, in neutral solution, gives a reddish-brown precipitate with the arsenate, and a yellow precipitate with the phosphate.

Tests for Impurities. *Lead.*—To the aqueous solution add ammonium hydroxide, potassium cyanide, and a drop of sodium sulphide solution. There should be no dark coloration. Under the conditions of the test, sodium arsenate gives no precipitate of arsenious sulphide, so that there is no interference.

Copper.—Add ammonium hydroxide to the aqueous solution and filter if necessary. The filtrate should have no blue tinge, and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Before testing the salt for the remaining metallic impurities, dissolve in a little dilute hydrochloric acid and dilute with water. Pass sulphur dioxide to reduce the arsenate to arsenite. Boil off the excess of sulphur dioxide and pass hydrogen sulphide to precipitate the arsenic, with any lead or copper, taking care that precipitation is complete. Filter, boil, and test the filtrate for the following metallic impurities:

Iron, Aluminium, and Calcium.—Test as described under Sodii Carbonas.

Carbonate.—The dry salt should not effervesce with dilute acids.

Sulphate and Chloride.—There should be no indication of these when a solution of the salt is tested as under Sodii Carbonas.

Nitrate.—Apply the brown ring test to the aqueous solution (p. 35).

Quantitative Estimation. (1) *Limit of Moisture.*—It should lose not more than 2 per cent of its weight when dried at 150°.

(2) The volumetric estimation consists in titrating with standard thiosulphate solution the iodine liberated from potassium iodide *in strongly acid solution* by the oxidising action of the arsenate. Weigh about 1 gramme, dissolve, and dilute to 100 mils. To portions of 20 mils add about 20 mils of strong hydrochloric acid, and about 2·5 grammes of potassium iodide. After allowing to stand for 10 minutes (in order that the liberation of iodine may be complete), titrate with N/10 sodium thiosulphate solution until colourless. Starch mucilage cannot be employed as indicator, owing to the presence of the concentrated acid :

$$2Na_2HAsO_4 + 4HCl = As_2O_5 + 4NaCl + 3H_2O,$$
$$KI + HCl = KCl + HI,$$
$$As_2O_5 + 4HI = As_2O_3 + 2H_2O + 2I_2.$$

$$2Na_2S_2O_3 + I_2 = Na_2S_4O_6 + 2NaI,$$
$$2Na_2S_2O_3,5H_2O \equiv I_2 \equiv Na_2HAsO_4,$$
$$2 \times 248 \equiv 186 \text{ grammes of } Na_2HAsO_4,$$
$$1000 \text{ mils of N/1 } Na_2S_2O_3,5H_2O \equiv 93 \text{ grammes of } Na_2HAsO_4,$$
$$1 \text{ mil N/10 } Na_2S_2O_3,5H_2O \equiv 0{\cdot}0093 \text{ gramme of } Na_2HAsO_4.$$

Liquor Sodii Arsenatis. *Solution of Sodium Arsenate.*—A simple 1 per cent *w/v* solution of anhydrous sodium arsenate. The anhydrous salt is used on account of the varying amount of water of crystallisation which the salt is liable to contain according to whether it is crystallised from hot solutions or cold. In the former case it crystallises with seven molecules of water, and in the latter case with twelve. Also, as there is a tendency for the salt with the higher amount of water to effloresce and become converted into that with the lower, it is evident that, were the crystalline salt permitted to be used, variation in the actual quantity of sodium arsenate in different samples of the solution might occur.

SODII ET POTASSII TARTRAS

Sodium Potassium Tartrate, $NaKC_4H_4O_6,4H_2O$. (Mol. Wt. = 282)
Syns. Rochelle Salt, Tartarated Soda

This is required to contain not less than 98 per cent of $NaKC_4H_4O_6,4H_2O$.

Preparation.—The salt is prepared by gradually adding two molecular proportions of finely powdered potassium hydrogen tartrate to a hot solution of one molecular proportion of sodium carbonate:

$$2KHC_4H_4O_6 + Na_2CO_3 = 2NaKC_4H_4O_6 + H_2O + CO_2.$$

The liquid is then filtered, and evaporated to crystallisation.

Properties.—Colourless, prismatic crystals, or a white crystalline powder, with a cooling, saline taste. Soluble 1-1·5 in water forming a neutral solution. On heating, it chars, evolving inflammable vapours and leaving a residue of sodium and potassium carbonates.

Tests for Impurities.—Ignite the salt, extract the residue with dilute hydrochloric acid, and filter. Test the filtrate for the metallic impurities.

Copper, Iron, and Calcium.—Test as under Sodii Carbonas.

Ammonium.—Boil some of the sodium potassium tartrate with sodium hydroxide, and test the evolved vapours with turmeric paper.

Chloride and Sulphate.—There should be no indication of these when a solution of the salt is tested as under Sodii Carbonas.

Lead Limit.—20 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—This salt is estimated by ignition, and titration of the alkaline residue in a manner similar to that described under Potassii Acetas, employing the same quantity of salt:

$$2NaKC_4H_4O_6 \longrightarrow Na_2CO_3 + K_2CO_3,$$
$$2H_2SO_4 + K_2CO_3 + Na_2CO_3 = K_2SO_4 + Na_2SO_4 + 2CO_2 + 2H_2O,$$
$$H_2SO_4 \equiv NaKC_4H_4O_6,4H_2O,$$
$$98 \equiv 282,$$
$$1000 \text{ mils } N/1\ H_2SO_4 \equiv 141 \text{ grammes of } NaKC_4H_4O_6,4H_2O,$$
$$1 \text{ mil } N/10\ H_2SO_4 \equiv 0{\cdot}0141 \text{ gramme of } NaKC_4H_4O_6,4H_2O.$$

Pulvis Sodæ Tartaratæ Effervescens. *Seidlitz Powder.*—Effervescent tartarated soda powder contains in No. 1 powder (blue paper) sodium potassium tartrate, 7·5 grammes, and sodium bicarbonate, 2·5 grammes. No. 2 powder (white paper) consists of tartaric acid, 2·5 grammes. The No. 1 powder is dissolved in cold or warm water, and No. 2 added, the liquid being taken during effervescence. The quantity of tartaric acid is sufficient to neutralise the bicarbonate and leave the solution slightly acid.

SODII BENZOAS

Sodium Benzoate, $C_6H_5 . COONa$. (Mol. Wt. = 144)

This is required to contain not less than 96 per cent of $C_6H_5 . COONa$.

Preparation.—*To a hot, concentrated solution of benzoic acid (p. 359)* sodium carbonate is gradually added until effervescence ceases. The salt is obtained either by crystallisation, or by cautious evaporation to dryness, and granulation :

$$2C_6H_5 . COOH + Na_2CO_3 = 2C_6H_5 . COONa + CO_2 + H_2O.$$

Properties.—A white, crystalline or granular amorphous powder with a sweetish, astringent taste, odourless, or having a faint odour of benzoin. Soluble 1-2 in water and 1-24 in alcohol, the aqueous solution being slightly alkaline to litmus. A cold, concentrated, aqueous solution, on treatment with dilute hydrochloric acid, yields a white crystalline precipitate of benzoic acid. When heated, the salt fuses and then decomposes, with evolution of inflammable vapours having an odour of benzoic acid, and leaves on ignition a residue of sodium carbonate and carbon.

Tests for Impurities (to be applied to the aqueous solution). *Copper and Iron.*—Test as described under Sodii Carbonas.

Potassium.—Apply the flame test to the dry salt, using an indigo prism.

Carbonate.—There should be no effervescence on the addition of dilute acid.

Sulphate and Chloride.—Add dilute nitric acid to the aqueous solution, filter from the precipitated benzoic acid, and test the filtrate as described under Sodii Carbonas.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—The salt is estimated by ignition, and titration of the alkaline residue as described under Potassii Acetas, using the same quantity :

$$2C_6H_5 . COONa \longrightarrow Na_2CO_3,$$
$$H_2SO_4 + Na_2CO_3 = Na_2SO_4 + CO_2 + H_2O,$$
$$H_2SO_4 = 2C_6H_5 . COONa,$$
$$98 \equiv 2 \times 144,$$
$$1000 \text{ mils } N/1\ H_2SO_4 \equiv 144 \text{ grammes of } C_6H_5 . COONa,$$
$$1 \text{ mil } N/10\ H_2SO_4 \equiv 0{\cdot}0144 \text{ gramme of } C_6H_5 . COONa.$$

SODII SALICYLAS

Sodium Salicylate, $C_6H_4(OH)COONa$. (Mol. Wt. = 160)

This is required to contain not less than 99·5 per cent of $C_6H_4(OH)COONa$.

Preparation.—A weighed amount of salicylic acid—natural or synthetic (p. 364)—is made into a paste with water, and slightly less than the theoretical quantity of pure sodium bicarbonate added :

$$C_6H_4(OH)COOH + NaHCO_3 = C_6H_4(OH)COONa + CO_2 + H_2O.$$

The solution of sodium salicylate so obtained is heated to expel carbon dioxide, strained if necessary, carefully evaporated to dryness at a low temperature, and the product purified by crystallisation from alcohol.

It is essential that the materials be very pure, and it is advisable to strain the solution through the finest muslin, rather than filter it through filter-paper, since the slightest trace of iron results in a discoloured product.

Properties.—If prepared from the natural acid it occurs as white pearly scales, or a white amorphous powder having a slight buff or pink tinge, and, possibly, an odour of methyl salicylate (p. 365). When prepared from the synthetic acid, however, it is free from colour and odour. Soluble 1·1 in water and 1·6 in alcohol (90 per cent). The aqueous solution is neutral or faintly acid to litmus, and, if sufficiently concentrated, yields on treatment with dilute mineral acids a white crystalline precipitate of salicylic acid. When the aqueous solution is mixed with a solution of sodium or potassium bicarbonates, or ammonium carbonate, a reddish-brown precipitate is produced in course of time, unless the salt is exceptionally pure. In dispensing, 1 grain of sodium bisulphite added to an 8-oz. mixture will retard this change, but the prescriber's sanction must of course be obtained. A saturated aqueous solution of sodium salicylate, on standing, may deposit crystals containing 6 molecules of water. On heating, sodium salicylate chars, evolving inflammable vapours and an odour of phenol, and on ignition a residue of sodium carbonate and carbon remains.

Tests for Impurities. *Carbonates.*—The salt should not be alkaline to litmus, and should not effervesce on treatment with dilute acids.

Sulphate and Chloride.—Acidify a concentrated aqueous solution with dilute nitric acid and filter from the precipitated salicylic acid. On diluting and testing separate portions of the filtrate with barium chloride and silver nitrate, there should not be more than the slightest turbidity or opalescence in either case.

Readily Carbonised Organic Impurities.—It should dissolve without coloration in concentrated sulphuric acid.

Free Phenol.—When the concentrated aqueous solution is shaken with an equal volume of ether and the ethereal layer is separated and allowed to evaporate spontaneously, the residue should be free from any odour of phenol (Squire).

The Pharmacopœia states that 50 to 100 grammes kept in a closed vessel for several days should not evolve the slightest odour of phenol.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—It is estimated by ignition and titration of the alkaline residue as described under Potassii Acetas, but employing about 2 grammes of the salt :

$$2C_6H_4(OH)COONa \longrightarrow Na_2CO_3,$$
$$H_2SO_4 + Na_2CO_3 = Na_2SO_4 + CO_2 + H_2O,$$
$$H_2SO_4 \equiv 2C_6H_4(OH)COONa,$$
$$98 \equiv 2 \times 160,$$
$$1000 \text{ mils } N/1 \; H_2SO_4 \equiv 160 \text{ grammes of } C_6H_4(OH)COONa,$$
$$1 \text{ mil } N/10 \; H_2SO_4 \equiv 0{\cdot}0160 \text{ gramme of } C_6H_4(OH)COONa.$$

COMPOUNDS OF LITHIUM

Li (Atomic Wt. = 7)

The salts of lithium are similar in general chemical properties to those of sodium and potassium. They are not so commonly employed in pharmacy, since, although lithium compounds are widely distributed in Nature, they are found in comparatively small quantities, and are therefore expensive. The chief source of lithium compounds is the mineral *lepidolite*, which has the composition $4LiF,K_2O,3Al_2O_3,9SiO_2$. The principal use of lithium salts in medicine is based upon the supposed removal of uric acid from the system as a readily soluble urate ; but, in the presence of sodium and potassium salts, the less soluble urates of these metals are formed, so that the efficacy of lithium salts in this connection is doubtful.

General Tests for Lithium.—(1) Lithium salts impart a crimson colour to the bunsen flame.

(2) Sodium carbonate yields with very concentrated solutions of lithium salts a white precipitate of lithium carbonate.

(3) Sodium phosphate, added to a fairly dilute solution of a lithium salt, produces no precipitate ; but on adding excess of sodium hydroxide, and boiling, a white precipitate is produced (distinction from magnesium).

LITHII CARBONAS

Lithium Carbonate, Li_2CO_3 (Mol. Wt. = 74)

This is required to contain not less than 98·5 per cent of Li_2CO_3.

Preparation.—Lithium carbonate may be prepared from lepidolite by fusing the mineral at a very high temperature with potassium sulphate, barium sulphate, and barium carbonate. The upper layer of the fused mass comprises potassium and lithium sulphates, which, after cooling, are extracted with water. From the solution, lithium carbonate is precipitated by the addition of ammonium carbonate.

Properties.—It occurs as a light, white, amorphous powder, or in crystalline grains, with a slightly alkaline taste. Soluble 1-80 in water, the solution being alkaline to litmus ; insoluble in alcohol (90 per cent).

Tests for Impurities (to be applied to the solution in dilute hydrochloric acid). *Copper.*—Add ammonium hydroxide in excess, and filter if necessary. The filtrate should have no blue tinge, and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—Add dilute nitric acid and potassium ferrocyanide. No blue or green colour should be produced.

Aluminium.—Add dilute nitric acid and boil, then add excess of sodium hydroxide, filter off any precipitate of ferric hydroxide, add excess of ammonium chloride to the filtrate, and again boil. No flocculent white precipitate should be produced.

Zinc.—Add ammonium chloride and ammonium hydroxide in excess, then pass hydrogen sulphide, when there should be no precipitate.

Calcium.—Add ammonium chloride and ammonium hydroxide in excess, followed by ammonium oxalate. There should be not more than the slightest precipitate.

Magnesium.—Add excess of ammonium hydroxide, and then add sodium phosphate. There should be no precipitate, even on shaking and allowing to stand.

Sulphate.—There should not be more than a slight turbidity on testing with barium chloride.

Chloride.—A solution of lithium carbonate in dilute nitric acid should yield no opalescence with silver nitrate.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—Lithium carbonate is estimated by neutralisation with standard sulphuric acid. Weigh about 1 gramme, suspend in about 50 mils of water, and titrate with N/1 sulphuric acid, very slowly, and with constant agitation, using methyl orange as indicator :

$$H_2SO_4 + Li_2CO_3 = Li_2SO_4 + CO_2 + H_2O,$$
$$98 \equiv 74,$$
$$1000 \text{ mils N/1 } H_2SO_4 \equiv 37 \text{ grammes of } Li_2CO_3,$$
$$1 \text{ mil N/1 } H_2SO_4 \equiv 0{\cdot}037 \text{ gramme of } Li_2CO_3.$$

LITHII CITRAS

Lithium Citrate, $Li_3C_6H_5O_7,4H_2O$. (Mol. Wt. = 282)

This is required to contain not less than 98·5 per cent of $Li_3C_6H_5O_7, 4H_2O$.

Preparation.—A solution of citric acid is neutralised with lithium carbonate, boiled, filtered, and concentrated to crystallisation :

$$2H_3C_6H_5O_7 + 3Li_2CO_3 = 2Li_3C_6H_5O_7 + 3CO_2 + 3H_2O.$$

Properties.—Small, colourless, deliquescent crystals with a saline taste. Soluble 1-2 in water. On heating, it loses three

molecules of water at 100°, and becomes completely dehydrated at 160°. At a red heat it chars, evolving inflammable vapours with a pungent odour, and leaving a residue of lithium carbonate and carbon.

Tests for Impurities.—This salt should be free from the impurities mentioned under Lithii Carbonas. The tests for metallic impurities should be applied to a solution obtained by igniting the salt, extracting the residue with dilute hydrochloric acid, and filtering. The tests for the non-metallic impurities may be applied to the aqueous solution.

Lead Limit.—5 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—It is estimated by ignition and titration of the alkaline residue, as described under Potassii Acetas, using the same quantity of salt. If it be ignited at too high a temperature, part of the carbonate may be decomposed with formation of the oxide. This will not, however, affect the result, since the lithium oxide produced will neutralise the same amount of acid as would the carbonate:

$$2Li_3C_6H_5O_7 \longrightarrow 3Li_2CO_3,$$
$$H_2SO_4 + Li_2CO_3 = Li_2SO_4 + CO_2 + H_2O,$$
$$3H_2SO_4 \equiv 2Li_3C_6H_5O_7,4H_2O,$$
$$3 \times 98 \equiv 2 \times 282,$$
$$1000 \text{ mils } N/1\ H_2SO_4 \equiv 94 \text{ grammes of } Li_3C_6H_5O_7,4H_2O,$$
$$1 \text{ mil } N/10\ H_2SO_4 \equiv 0{\cdot}0094 \text{ gramme of } Li_3C_6H_5O_7,4H_2O.$$

Lithii Citras Effervescens. *Effervescent Lithium Citrate.*—A mixture of lithium citrate, citric acid, tartaric acid, and sodium bicarbonate is heated on a water-bath, and the pasty mass forced through a sieve to produce granules of uniform size, the product being dried below 55° (see Sodii Phosphas Effervescens).

COMPOUNDS OF AMMONIUM

Ammonium salts are derived from ammonium hydroxide, which is formed when ammonia gas is dissolved in water:

$$NH_3 + H_2O = NH_4OH.$$

The radicle ammonium, NH_4-, behaves like a univalent metal, and the ammonium salts, being similar in chemical properties to the salts of the alkali metals, may be considered conveniently here. The ammonium salts in general differ from the salts of the alkali metals in being readily volatilised by heat, and in being appreciably hydrolysed in aqueous solution.

Ammonium compounds are obtained from two principal sources:

(1) From the "ammoniacal liquor" of the gas works (p. 32).

(2) From atmospheric nitrogen.

Nitrogen can be "fixed" as ammonia in several ways, some of which are patented or secret processes. In one process, a mixture

of lime and coke is heated in an electric furnace in an atmosphere of nitrogen, when calcium cyanamide is produced :

$$CaO + 2C + N_2 = \underset{\text{Calcium cyanamide.}}{CaN.CN} + CO.$$

Ammonia may be obtained from this by heating with water under pressure :

$$CaN.CN + 3H_2O = CaCO_3 + 2NH_3.$$

A more direct method of obtaining ammonia is that of Haber, in which atmospheric nitrogen is made to combine with hydrogen by passing the mixed gases over suitable catalysts, for example, metallic iron, at a high temperature :

$$N_2 + 3H_2 = 2NH_3.$$

Ammonia prepared by any of these methods can be converted into ammonium salts by neutralisation with acids.

The chief commercial salt of ammonium is the sulphate, $(NH_4)_2SO_4$, which is manufactured by absorbing in sulphuric acid the gas liberated from ammoniacal gas liquor.

General Tests for Ammonium.—(1) On heating, ammonium salts volatilise, leaving no residue.

(2) When heated with alkalies, ammonium salts or their solutions evolve ammonia gas, which may be recognised by its odour and its action on turmeric paper (p. 32).

(3) A concentrated solution of an ammonium salt yields with tartaric acid a crystalline precipitate of sparingly soluble ammonium hydrogen tartrate, $NH_4HC_4H_4O_6$.

AMMONII CARBONAS

Ammonium Carbonate. *Unofficial Syn.* Sal Volatile

This is a variable mixture of ammonium hydrogen carbonate, NH_4HCO_3, and ammonium carbamate, $NH_4NH_2CO_2$ (p. 310), and is required to contain 30·6 per cent of ammonia, calculated as NH_3.

Preparation.—This substance is prepared by heating an ammonium salt with calcium carbonate and collecting the resulting sublimate. In practice, ammonium sulphate is most commonly used on account of its cheapness. The first reaction may be regarded as a case of simple double decomposition, normal ammonium carbonate being produced :

$$(NH_4)_2SO_4 + CaCO_3 = CaSO_4 + (NH_4)_2CO_3.$$

But normal ammonium carbonate is a very unstable substance when not in solution, and decomposes with loss of ammonia and water, thus :

$$(NH_4)_2CO_3 = NH_4HCO_3 + NH_3,$$
$$(NH_4)_2CO_3 = NH_4NH_2CO_2 + H_2O.$$

Two molecules yield one molecule of ammonium hydrogen carbonate and one of ammonium carbamate. The product is purified by resublimation with a small quantity of water.

Properties.—Translucent masses with a striated appearance and an ammoniacal odour and taste. Soluble 1-4 in water, 1-200 in alcohol (90 per cent). The aqueous solution is alkaline to litmus and contains normal carbonate, owing to the combination of water with the carbamate. Alcohol dissolves the carbamate readily, the hydrogen carbonate being much less soluble. Hot water decomposes ammonium carbonate with evolution of ammonia and carbon dioxide, so that when a solution is required it should be made in cold water. On exposure to air, the substance slowly loses ammonia and carbon dioxide, leaving an opaque coating of ammonium hydrogen carbonate which must be scraped off before use in dispensing. When heated, it sublimes completely.

Tests for Impurities. *Sulphate.*—A solution in excess of dilute nitric acid should yield not more than a slight turbidity with barium chloride.

Chloride.—A similar solution should yield not more than a faint opalescence with silver nitrate.

Tarry Matter.—The aqueous solution, neutralised with a mineral acid, and evaporated to dryness, should leave a colourless and odourless residue.

Lead Limit.—5 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—The substance is estimated by neutralisation with normal sulphuric acid, the strength being calculated in terms of ammonia, NH_3. Weigh about 4 grammes, dissolve in cold water, dilute to 100 mils, and titrate portions of 20 mils with N/1 sulphuric acid, using methyl orange as indicator. The following reactions occur :

$$NH_4NH_2CO_2 + H_2O = (NH_4)_2CO_3,$$

the normal carbonate being then neutralised, thus :

$$(NH_4)_2CO_3 + H_2SO_4 = (NH_4)_2SO_4 + CO_2 + H_2O.$$

The ammonium hydrogen carbonate in the substance is neutralised according to the equation :

$$2NH_4HCO_3 + H_2SO_4 = (NH_4)_2SO_4 + 2H_2O + 2CO_2.$$

The calculation may be based upon the equation :

$$\begin{gathered} H_2SO_4 + 2NH_3 = (NH_4)_2SO_4, \\ 98 \equiv 2 \times 17, \\ 1000 \text{ mils N/1 } H_2SO_4 \equiv 17 \text{ grammes of } NH_3, \\ 1 \text{ mil N/1 } H_2SO_4 \equiv 0{\cdot}017 \text{ gramme of } NH_3. \end{gathered}$$

SPIRITUS AMMONIÆ AROMATICUS

Aromatic Spirit of Ammonia. *Syn.* Spirit of Sal Volatile.

Preparation.—Oils of lemon and nutmeg are placed in a retort and distilled with alcohol. The first portion of the distillate, a strongly alcoholic solution of the oils, is reserved; a second, much smaller and largely aqueous, portion is then collected separately, placed in a securely stoppered bottle, together with solution of ammonia and ammonium carbonate, and warmed in a water-bath at 60° until the solid has dissolved. The contents of the bottle are then strained through cotton-wool, and added gradually to the alcoholic solution of the oils first distilled.

It might be thought that it would suffice to dissolve the oils in the alcohol without distillation, but such a procedure results in a product liable to rapid discoloration by oxidation and action of the alkali on the oils.

Quantitative Estimations.—(1) The first test is for total ammonia by titration with N/1 H_2SO_4, using methyl orange as indicator, and requires no comment except that it is advisable to add a known excess of acid and back-titrate with N/1 sodium hydroxide to obtain accurate results (p. 33).

(2) The second test is for the amount of ammonium hydrogen carbonate and ammonium carbamate present, calculated together as $NH_4HCO_3,NH_4NH_2CO_2$, as, should this substance have been omitted and ammonium hydroxide substituted, there would be no indication from a simple titration, as in the first test. Dilute 20 mils of the spirit and mix with excess of barium chloride solution, heating the mixture to 70° in order to render granular the precipitate of barium carbonate which is formed. Collect the precipitate on a filter, wash until free from ammonia, and dissolve in 20 mils of N/1 hydrochloric acid. After boiling (to drive off carbon dioxide) and cooling, determine the amount of acid used by titration of the excess with N/1 sodium hydroxide, using methyl orange as indicator:

$$NH_4HCO_3,NH_4NH_2CO_2 + NH_4OH = 2(NH_4)_2CO_3,$$
$$2(NH_4)_2CO_3 + 2BaCl_2 = 2BaCO_3 + 4NH_4Cl,$$
$$2BaCO_3 + 4HCl = 2BaCl_2 + 2CO_2 + 2H_2O,$$
$$\therefore 4HCl \equiv 2BaCO_3 \equiv NH_4HCO_3,NH_4NH_2CO_2,$$
$$4 \times 1000 \text{ mils N/1 HCl} \equiv 157{\cdot}0 \text{ grammes of } NH_4HCO_3,NH_4NH_2CO_2,$$
$$1 \text{ mil N/1 HCl} \equiv 0{\cdot}0392 \text{ gramme of } NH_4HCO_3,NH_4NH_2CO_2.$$

Spiritus Ammoniæ Fetidus. *Fetid Spirit of Ammonia.*—This is prepared by maceration of the oleo-gum-resin asafetida for twenty-four hours in alcohol in order to dissolve out the volatile oil, followed by distillation on a water-bath. The distillate is adjusted to the required volume by the addition of Strong Solution of Ammonia and alcohol.

Quantitative Estimation.—The spirit is required to contain not less than 2·72 grammes of ammonia, NH_3, in 100 mils. Add 40 mils of N/1 sulphuric acid to 10 mils of the spirit and determine the quantity used by titrating the excess with N/1 sodium hydroxide, using methyl orange as indicator (p. 33).

AMMONII CHLORIDUM

Ammonium Chloride, NH_4Cl. (Mol. Wt. = 53·5)

Preparation.—This may be prepared by neutralising ammonium hydroxide with hydrochloric acid and evaporating to dryness. It is manufactured from ammoniacal liquor (p. 32) by this method :

$$NH_3 + HCl = NH_4Cl.$$

The product, which forms tough, fibrous, crystalline masses, and which is commonly called *sal ammoniac*, is purified for pharmaceutical purposes by sublimation from iron vessels.

Properties.—A colourless, odourless, crystalline powder with a saline taste. Soluble 1-3 in water, 1-60 in alcohol (90 per cent). On heating it volatilises completely, and can be recovered unchanged as a sublimate.

Tests for Impurities (to be applied to the aqueous solution). *Copper.*—Add excess of ammonium hydroxide and filter from any precipitate. The filtrate should have no blue tinge, and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—There should be not more than the slightest blue or green coloration on the addition of nitric acid and potassium ferrocyanide.

Carbonate.—There should be no precipitate on the addition of calcium chloride solution.

Sulphate.—Acidify with hydrochloric acid and add barium chloride. There should not be more than a slight turbidity.

Nitrate.—Apply the brown ring test (p. 35).

Lead Limit.—5 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

AMMONII BROMIDUM

Ammonium Bromide, NH_4Br. (Mol. Wt. = 98)

When dried at 100° this is required to contain not less than 98 per cent of NH_4Br.

Preparation.—(1) The salt may be prepared by neutralising a solution of hydrobromic acid with ammonium hydroxide and evaporating to crystallisation :

$$HBr + NH_4OH = NH_4Br + H_2O.$$

(2) It is manufactured by the action of ammonium carbonate

on iron bromide in a manner similar to that described under Potassii Bromidum.

Properties.—Colourless crystals, or a white crystalline powder, with a saline, somewhat pungent taste. Soluble 1-1·5 in water, 1-13 in alcohol (90 per cent). On heating it volatilises.

Tests for Impurities (to be applied to the aqueous solution). *Iron.*—Acidify with nitric acid and test with potassium ferrocyanide, when there should be no blue or green coloration.

Sulphate.—Acidify with hydrochloric acid and test with barium chloride. There should be no more than a slight turbidity.

Bromate.—(1) Add silver nitrate in excess, boil, and filter. No crystalline precipitate of silver bromate should be deposited from the filtrate when allowed to stand until cold. (2) Add to the solution of the salt, potassium iodide, some starch mucilage, and a few drops of dilute sulphuric acid. There should be no blue colour.

Iodide.—Add to the aqueous solution dilute sulphuric acid, a crystal of sodium nitrite, and some starch mucilage. There should be no blue colour.

Nitrate.—Add dilute sulphuric acid, starch mucilage, and potassium iodide; then add a scrap of zinc. There should be no blue colour.

Non-volatile Solids.—The dry salt should volatilise completely on ignition.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—(1) The salt should lose not more than 1 per cent of its weight when dried at 100°.

(2) The volumetric estimation is based upon the precipitation of the bromide as silver salt, potassium chromate being used as indicator (see Potassii Bromidum).[1] Weigh about 1 gramme, dissolve, and dilute to 100 mils. To portions of 20 mils add a few drops of potassium chromate solution, and titrate with N/10 silver nitrate solution until a permanent red precipitate is produced:

$$AgNO_3 + NH_4Br = AgBr + NH_4NO_3,$$
$$170 \equiv 98,$$
$$1000 \text{ mils N/1 } AgNO_3 \equiv 98 \text{ grammes of } NH_4Br,$$
$$1 \text{ mil N/10 } AgNO_3 \equiv 0{\cdot}0098 \text{ gramme of } NH_4Br.$$

LIQUOR AMMONII ACETATIS

Solution of Ammonium Acetate

Ammonium acetate is an unstable salt, and is therefore included in the Pharmacopœia only in the form of its solution.

[1] The Pharmacopœia states that 0·5 gramme of the dried salt requires for complete precipitation not less than 50·5 and not more than 51·5 mils of N/10 silver nitrate. A higher titration value would indicate the presence of an undue proportion of chloride as impurity.

Preparation.—Acetic acid, 162·5 parts, is diluted with 500 parts of water and neutralised with ammonium carbonate, according to the equation:

$$NH_4HCO_3,NH_4NH_2CO_2 + 3CH_3 . COOH = 3CH_3 . COONH_4 + 2CO_2 + H_2O.$$

The acid requires more carbonate than the quantity suggested in the Pharmacopœia. It is not possible to determine the point of neutrality by means of litmus paper, owing to the quantity of carbon dioxide evolved, which would affect the indicator; nor is it permissible to expel the carbon dioxide by heating the solution, since this results in the decomposition of the ammonium acetate. It is customary, therefore, to add a drop of the solution from time to time, alternately, to crystals of potassium bicarbonate and citric acid exposed on a glass plate or porcelain tile; when the solution ceases to effervesce with either crystal it may be accepted as neutral and the volume adjusted to 1000 parts with water. On the large scale it is more usual to determine the strength of the acid and carbonate by titration and to mix them in the correct proportions. It is essential that the ammonium carbonate and acid used should be the purest possible, or the solution tends to have a distinct foreign odour; this is especially noticeable when the solution is prepared in the concentrated (1 to 7) form. Specific gravity, 1·016.

Test for Impurities. *Heavy Metals* (*Limit of*).—When mixed with an equal volume of a saturated aqueous solution of hydrogen sulphide not more than the slightest darkening in colour should result.

LIQUOR AMMONII CITRATIS

Solution of Ammonium Citrate

Ammonium citrate is only included in the Pharmacopœia in the form of its solution. The solution is prepared in precisely the same manner as the solution of ammonium acetate, neutralising 125 parts of citric acid in 625 parts of water by means of ammonium carbonate, and adjusting the volume to 1000 parts with water:

$$NH_4HCO_3,NH_4NH_2CO_2 + H_3C_6H_5O_7 = (NH_4)_3C_6H_5O_7 + 2CO_2 + H_2O.$$

The same test for neutrality is used as described under Liquor Ammonii Acetatis. Specific gravity, 1·057.

Test for Impurities. *Heavy Metals* (*Limit of*).—Test as under Liquor Ammonii Acetatis.

NOTE.—Solutions of ammonium acetate and ammonium citrate should be preserved in bottles the glass of which is free from lead (green glass), as the solutions have the property of dissolving certain lead salts.

AMMONII BENZOAS

Ammonium Benzoate, $C_6H_5.COONH_4$. (Mol. Wt. = 139)

Preparation.—This salt may be prepared by dissolving benzoic acid—natural or synthetic (p. 359)—in a slight excess of dilute ammonium hydroxide and carefully evaporating at a gentle heat, adding sufficient ammonium hydroxide from time to time to maintain a slight excess of the alkali :

$$C_6H_5.COOH + NH_4OH = C_6H_5.COONH_4 + H_2O.$$

If an excess of ammonia is not maintained during the evaporation some free benzoic acid is formed, and the employment of even moderate temperature in drying the salt results in its decomposition.

Properties.—White, scaly crystals with a saline, slightly acrid taste. Soluble 1-6 in water, 1-30 in alcohol (90 per cent). The addition of hydrochloric acid to a concentrated aqueous solution produces a white, crystalline precipitate of benzoic acid. On heating it first fuses, then decomposes with evolution of ammonia and vapours of benzoic acid, and finally completely volatilises. On keeping, ammonium benzoate acquires an acid reaction due to decomposition and loss of ammonia, becoming less soluble.

Tests for Impurities. *Sulphate and Chloride.*—When 1 gramme is dissolved in 20 mils of water and excess of nitric acid added, a crystalline precipitate of benzoic acid separates. If the liquid be filtered the filtrate should give not more than a faint opalescence on the addition of silver nitrate to one portion (absence of more than a trace of chloride), and should remain clear on the addition of barium chloride to another portion (absence of sulphate).

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

CHAPTER VII

COMPOUNDS OF CALCIUM AND STRONTIUM

COMPOUNDS OF CALCIUM

Ca (Atomic Wt. = 40)

CALCIUM does not occur in Nature in the free state, but is found in very large quantities in the form of its carbonate, $CaCO_3$, in such minerals as *marble*, *limestone*, and *calcspar*, and associated with magnesium carbonate in *dolomite*. Calcium sulphate occurs as *gypsum*, $CaSO_4,2H_2O$, and as *anhydrite*, $CaSO_4$; the fluoride, CaF_2, occurs as *fluorspar*; and bones contain a high percentage of calcium phosphate. Several calcium compounds, when purified, are important pharmaceutical substances.

General Tests for Calcium.—(1) The addition of ammonium chloride and ammonium hydroxide, followed by ammonium carbonate, to a solution of a calcium salt, produces a bulky precipitate of calcium carbonate, which on boiling becomes granular and distinctly crystalline.

(2) Ammonium oxalate, added to a neutral or alkaline solution of a calcium salt, produces a white precipitate of calcium oxalate, insoluble in acetic acid, but soluble in hydrochloric acid.

(3) Dilute sulphuric acid, added to a concentrated solution of a calcium salt, produces a precipitate of calcium sulphate, but in dilute solutions this does not appear (distinction from barium and strontium).

(4) A calcium salt, moistened with hydrochloric acid, imparts a brick-red colour to the bunsen flame, appearing green through an indigo prism.

CALX

Lime, CaO. (Mol. Wt. = 56)

Preparation.—Lime, quicklime, or calcium oxide is obtained by "burning" limestone or chalk with coal in lime-kilns:

$$CaCO_3 = CaO + CO_2.$$

Properties.—White or greyish lumps, which on moistening with water evolve much heat, and fall to a powder with formation of the

hydroxide. The moistened substance is alkaline to indicators and has a caustic taste. On exposure to air, quicklime rapidly absorbs water and carbon dioxide with formation of calcium hydroxide and carbonate.

Tests for Impurities. *Iron.*—Dissolve in nitric acid and add potassium ferrocyanide, when there should not be more than a slight blue or green coloration.

Carbonate.—There should not be more than the slightest effervescence on the addition of a mineral acid to a little of the lime, previously slaked with water and allowed to cool.

Sulphate.—Dissolve in dilute nitric acid and test with barium chloride. There should be no more than a slight turbidity.

Chloride.—The nitric acid solution should not give more than a slight opalescence with silver nitrate.

Silica.—Heat to redness in a nickel crucible with sodium carbonate and allow to cool; extract the mass with water, filter, and acidify the solution with concentrated hydrochloric acid, when there should be no precipitate.

Lime should be almost completely soluble in hydrochloric acid.

Arsenic Limit.—5 parts per million (p. 176).

CALCII HYDRAS

Calcium Hydroxide, $Ca(OH)_2$. (Mol. Wt. = 74.)
Unofficial Syn. Slaked Lime

Preparation.—Calcium hydroxide is prepared by slaking the oxide, lime, with water:

$$CaO + H_2O = Ca(OH)_2.$$

The addition of water results in the generation of considerable heat. In practice, an excess of water is added and the supernatant liquid decanted, this serving to remove the greater portion of any soluble impurities.

Properties.—A white, or nearly white, odourless powder, with a caustic taste. Soluble 1·900 in cold water, less soluble in hot water. The aqueous solution has an alkaline reaction, and, on exposure to air, deposits a precipitate of calcium carbonate due to absorption of atmospheric carbon dioxide. The solid substance undergoes a similar change, and for this reason must be stored in stoppered bottles. On heating, the hydroxide loses water and becomes reconverted into the oxide.

Tests for Impurities.—Test as described under Calx.

Lead Limit.—20 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Test for Strength.—On heating a weighed quantity to redness

in a crucible, calcium hydroxide should lose nearly one-fourth its weight of water.

LIQUOR CALCIS

Solution of Lime

Syn. Lime Water

Preparation.—Calcium hydroxide is washed free from chloride, and a large excess of it shaken with distilled water in a stoppered, lead-free (green glass) bottle for several minutes. When required for use, the saturated, supernatant liquid is removed by means of a siphon. Each time the solution is exposed to air, atmospheric carbon dioxide precipitates a little of the calcium as carbonate; for this reason no more should be siphoned off than is required for immediate use.

Tests for Impurities. *Lead.*—Add ammonium hydroxide and potassium cyanide solution, then a drop of sodium sulphide solution, when there should be no coloration.

Chloride.—Acidify with nitric acid and test with silver nitrate solution, when there should be no opalescence.

Quantitative Estimation.—The solution is estimated by neutralisation with standard acid. Titrate portions of 40 mils with N/10 sulphuric acid, using methyl orange as indicator. It should contain rather more than 0·1 per cent *w/v* of lime, calculated as CaO :

$$H_2SO_4 + CaO = CaSO_4 + H_2O,$$
$$98 \equiv 56,$$
$$1000 \text{ mils N/1 } H_2SO_4 \equiv 28 \text{ grammes of CaO},$$
$$1 \text{ mil N/10 } H_2SO_4 \equiv 0{\cdot}0028 \text{ gramme of CaO}.$$

Liquor Calcis Saccharatus. *Saccharated Solution of Lime.*—The preparation of this solution is based upon the greatly increased solubility of lime in sugar solution owing to the formation of a loosely combined compound called calcium saccharosate.[1] The lime, 50 parts, is shaken occasionally during a few hours in a green glass bottle with a solution of 100 parts of refined sugar (sucrose) in 1000 parts of water. The solution is siphoned off, guarding against unnecessary exposure to air, in order to prevent the formation of carbonate as far as possible. The lime is not previously washed free from chloride in this case as the solution is not used in any official preparation.

Test for Impurity. Lead.—Test as under Liquor Calcis.

Quantitative Estimation.—This solution is estimated as described under Liquor Calcis, titrating portions of 20 mils with N/1 sulphuric acid. It should contain nearly 2 per cent of lime, calculated as CaO.

[1] $C_{12}H_{22}O_{11} . Ca(OH)_2, H_2O$.

CRETA PRÆPARATA

Prepared Chalk

Calcium Carbonate, $CaCO_3$. (Mol. Wt. = 100)

This substance is native calcium carbonate, or chalk, freed from gritty impurities by elutriation.

Preparation.—The natural chalk is ground into fine powder and made into a paste with water. A large quantity of water is then added and, after stirring briskly, the supernatant liquid is decanted, carrying with it the fine particles. Further quantities of water are added to the residue, and the stirring and decantation repeated. The decanted liquors are mixed and allowed to stand, and the sediment is collected, partially dried, and then the pasty mass is formed into the familiar cones by trochiscation, *i.e.* by shaking small portions of the paste out on to a porous slab from a conical container.

Properties.—White, or greyish white, friable masses, or a white powder, having a darker and coarser appearance than precipitated chalk, from which it is readily distinguishable. It dissolves in dilute nitric, hydrochloric, or acetic acid, leaving not more than a slight residue.

Tests for Impurities.—The tests for metallic impurities are to be applied to the solution in dilute hydrochloric acid.

Iron.—Add nitric acid and potassium ferrocyanide, when not more than a slight blue or green coloration should be produced.

Aluminium.—Add excess of sodium hydroxide, filter off any precipitate, add excess of ammonium chloride, and boil. There should be no appreciable precipitate.

Magnesium.—Add ammonium chloride and ammonium hydroxide in excess, followed by ammonium carbonate. Filter off the precipitate of calcium carbonate, and add to the filtrate sodium phosphate, when there should be no immediate precipitate.

Sulphate.—A solution in dilute hydrochloric acid should yield not more than a slight turbidity with barium chloride.

Phosphate.—A solution in nitric acid should give no yellow precipitate when warmed with excess of ammonium molybdate.

Silica.—Test as described under Calx.

Barium Carbonate.—The Pharmacopœia prescribes the following test. Dissolve in dilute acetic acid and add potassium chromate, when there should be no precipitate.

Arsenic Limit.—5 parts per million (p. 176).

CALCII CARBONAS PRÆCIPITATUS

Precipitated Calcium Carbonate, $CaCO_3$. (Mol. Wt. = 100.)

Syn. Precipitated Chalk

Preparation.—Boiling solutions of calcium chloride and sodium carbonate are mixed, and the resulting precipitate allowed to

subside, collected on a calico filter, and washed with boiling water to remove chloride :

$$CaCl_2 + Na_2CO_3 = CaCO_3 + 2NaCl.$$

Properties.—A fine white powder, seen to be crystalline under the microscope. It dissolves in acids with considerable effervescence and evolution of carbon dioxide.

Tests for Impurities.—The tests for metallic impurities are to be applied to a solution in dilute hydrochloric acid.

Iron and Aluminium.—There should be no indication of these on testing as described under Creta Præparata.

Magnesium.—There should not be more than the slightest reaction when tested as under Creta Præparata.

Sulphate and Phosphate.—There should be no indication of these when tested as under Creta Præparata.

Chloride.—The addition of silver nitrate to a nitric acid solution of the carbonate should not produce more than a faint opalescence.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

CALCII CHLORIDUM

Calcium Chloride, $CaCl_2$ (Mol. Wt. = 111)

Preparation.—Calcium chloride is a by-product in numerous chemical processes, but for pharmaceutical use it is best prepared by acting upon chalk or marble with a slight excess of hydrochloric acid :

$$CaCO_3 + 2HCl = CaCl_2 + CO_2 + H_2O.$$

The liquid is evaporated to dryness, and the residue heated to a temperature not exceeding 200° to expel water, of which the resulting product should not contain more than 2 per cent.

Properties.—White, slightly translucent masses, very deliquescent on exposure to the atmosphere. Its property of absorbing moisture is frequently made use of in the drying of gases and the removal of extraneous water from other substances. Soluble 1-1·5 in water, 1-3 in alcohol (90 per cent). It fuses below a red heat and solidifies on cooling without change in composition.

Tests for Impurities (to be applied to the aqueous solution). *Iron and Aluminium.*—There should be no indication of these when tested as described under Creta Præparata.

Magnesium.—There should not be more than the slightest reaction for this when tested as under Creta Præparata.

Carbonate and Hypochlorite.—There should be no effervescence on moistening the dry salt with dilute hydrochloric acid, nor should any odour of chlorine be detectable.

Lead Limit.—20 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Test.—The only quantitative test given in the Pharmacopœia is for the amount of water present, it being stated that it should lose not more than 5 per cent of its weight when dried at 200°. Rapidly weigh about 1 gramme of the salt in a crucible and heat over a small flame, cooling the crucible in a desiccator and weighing from time to time until the weight is constant.

CALX SULPHURATA

Sulphurated Lime

This is a mixture consisting chiefly of calcium sulphide and calcium sulphate, and is required to contain not less than 50 per cent of CaS.

Preparation.—A mixture of calcium sulphate 70 parts, charcoal 10 parts, and starch 2 parts, is packed lightly into a crucible, covered loosely, and heated to bright redness until the contents have lost their black colour. Part of the calcium sulphate remains unchanged, and part is reduced by the carbon:

$$CaSO_4 + 4C = CaS + 4CO.$$

The product is allowed to cool, powdered, and rapidly transferred to a well-stoppered bottle.

Properties.—A greyish-white, amorphous powder, having an odour of hydrogen sulphide and a nauseous taste. Sparingly soluble in water, forming an alkaline solution. On exposure to air it slowly decomposes owing to the action of atmospheric moisture and carbon dioxide:

$$CaS + 2H_2O = Ca(OH)_2 + H_2S,$$
$$Ca(OH)_2 + CO_2 = CaCO_3 + H_2O.$$

On treatment with dilute hydrochloric acid, the calcium sulphide dissolves with evolution of hydrogen sulphide, leaving a residue of calcium sulphate and possibly traces of carbon.

Quantitative Test.—This depends upon the precipitation of copper sulphide from copper sulphate solution by the hydrogen sulphide liberated from Calx Sulphurata by the action of dilute hydrochloric acid:

$$CaS + 2HCl = CaCl_2 + H_2S,$$
$$H_2S + CuSO_4 = CuS + H_2SO_4.$$

Weigh 0·8 gramme and mix in a stoppered flask with a cold solution of 1·4 grammes of copper sulphate in about 50 mils of water. Add about 10 mils of dilute hydrochloric acid, heat nearly to boiling, shake well for ten minutes, and filter. The filtrate should give no reddish-brown colour with potassium ferrocyanide, showing that all the copper has been precipitated (presence of a due proportion of sulphide).

CALCII PHOSPHAS

Calcium Phosphate, $Ca_3(PO_4)_2$. (Mol. Wt. = 310)

Preparation.—(1) This may be obtained from bone-ash by extracting with dilute hydrochloric acid, filtering, and precipitating from the filtrate by the addition of excess of ammonia.

(2) For pharmaceutical purposes, it is best prepared by adding a boiling solution of calcium chloride to a boiling solution of disodium hydrogen phosphate containing some ammonia. The liquid is allowed to cool, the precipitate washed by decantation, collected on a filter, and again washed until free from chloride.

$$2Na_2HPO_4 + 3CaCl_2 + 2NH_4OH = Ca_3(PO_4)_2 + 4NaCl + 2NH_4Cl + 2H_2O.$$

Properties.—A light, white, amorphous, non-hygroscopic powder, without odour or taste. Almost insoluble in water, although water shaken with it may acquire a faintly acid reaction, due to traces of acid phosphate. Soluble in dilute mineral acids owing to the formation of acid phosphate :

$$Ca_3(PO_4)_2 + 2HCl \rightleftharpoons 2CaHPO_4 + CaCl_2,$$
$$Ca_3(PO_4)_2 + 4HCl \rightleftharpoons Ca(H_2PO_4)_2 + 2CaCl_2.$$

It is only very slightly soluble in acetic acid.

Tests for Impurities. *Carbonate, Silica, and Insoluble Matter.*—It should dissolve without effervescence, and without residue, in dilute hydrochloric or nitric acid.

Lead, Copper, and Iron.—The solution in dilute hydrochloric acid should not be darkened by hydrogen sulphide (absence of lead and copper), and the subsequent addition of excess of ammonium hydroxide produces a precipitate which should be quite white (limit of iron).

Before testing for other metallic impurities, remove the phosphate from a solution of the salt in dilute hydrochloric acid by adding ammonium chloride, almost neutralising with ammonium hydroxide, then adding excess of freshly prepared ammonium acetate, followed by ferric chloride, drop by drop, until a permanent reddish coloration is obtained. Boil for a few minutes and then filter.

Aluminium.—Boil the *residue* from the above phosphate separation with sodium hydroxide, dilute, filter, and add to the filtrate excess of ammonium chloride, then boil. There should be no white precipitate.

Barium.—To the *filtrate* from the phosphate separation add excess of ammonium hydroxide and ammonium carbonate. Filter off the precipitate, dissolve in acetic acid, and add potassium chromate. There should be no yellow precipitate.

Magnesium.—To the filtrate after the addition of ammonium carbonate in the barium test, add sodium phosphate, shake, and

allow to stand. There should not be more than the slightest precipitate.

Ammonium.—Dissolve some of the salt in dilute hydrochloric acid, add sodium hydroxide in excess, and boil. There should be no indication of ammonia on testing the evolved vapours with turmeric paper (p. 32).

Limit of Chloride and Sulphate.—The solution in dilute nitric acid should not be rendered more than slightly opalescent by the addition of silver nitrate to one portion, and should yield not more than a slight turbidity on the addition of barium chloride to another portion.

Arsenic Limit.—5 parts per million (p. 176).

CALCII HYPOPHOSPHIS

Calcium Hypophosphite, $Ca(H_2PO_2)_2$. (Mol. Wt. = 170)

This is required to contain not less than 98 per cent of $Ca(H_2PO_2)_2$.

Preparation.—The salt is prepared by boiling yellow phosphorus with milk of lime until phosphine ceases to be evolved. As the mixture of phosphine and other hydrides of phosphorus produced during this reaction is spontaneously inflammable, it is necessary to conduct the operation with special precautions :

$$8P + 3Ca(OH)_2 + 6H_2O = 3Ca(H_2PO_2)_2 + 2PH_3.$$

The liquid is filtered and the filtrate concentrated to crystallisation.

Properties.—A white crystalline powder with a nauseous, bitter taste. Soluble 1-8 in water, insoluble in alcohol (90 per cent). On heating, it decrepitates and at about 300° commences to decompose, evolving water vapour and a spontaneously inflammable mixture of phosphine, other hydrides of phosphorus, and hydrogen, leaving a residue of calcium metaphosphate, with some pyrophosphate and a little red phosphorus.

Calcium hypophosphite is a powerful reducing agent ; for this reason it is incompatible with oxidising agents and requires especial care in dispensing. It reduces mercuric chloride, first to mercurous chloride, and finally to metallic mercury ; and it precipitates metallic silver from solutions of its salts.

Tests for Impurities (to be applied to the aqueous solution). *Copper.*—Add nitric acid, warm, and then add excess of ammonium hydroxide and filter. The filtrate should have no blue tinge, and on acidifying with acetic acid and adding potassium ferrocyanide should give no brown coloration.

Iron.—A little of the solution, warmed with dilute nitric acid, should give no blue or green coloration with potassium ferrocyanide.

Sulphate.—There should not be more than a slight turbidity on the addition of hydrochloric acid and barium chloride.

Chloride.—The addition of nitric acid and silver nitrate should produce not more than a faint opalescence.

Phosphate and Phosphite.—Though not mentioned in the British Pharmacopœia of 1914, these are amongst the most common impurities in the salt. The aqueous solution should yield not more than a slight precipitate with lead acetate.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—The salt is estimated in exactly the same manner as described under Sodii Hypophosphis:

$$Ca(H_2PO_2)_2 + H_2SO_4 = CaSO_4 + 2H_3PO_2,$$
$$2K_2Cr_2O_7 + 3H_3PO_2 + 8H_2SO_4 = 2K_2SO_4 + 2Cr_2(SO_4)_3 + 3H_3PO_4 + 8H_2O,$$
$$4K_2Cr_2O_7 \equiv 3Ca(H_2PO_2)_2,$$
$$4 \times 294 \equiv 3 \times 170,$$
$$1000 \text{ mils } N/1\ K_2Cr_2O_7 \equiv 21{\cdot}25 \text{ grammes of } Ca(H_2PO_2)_2,$$
$$1 \text{ mil } N/10\ K_2Cr_2O_7 \equiv 0{\cdot}002125 \text{ gramme of } Ca(H_2PO_2)_2.$$

CALCII LACTAS

Calcium Lactate, $[CH_3.CH(OH).COO]_2Ca,5H_2O$
(Mol. Wt. = 308)

This is required to contain not less than 93 per cent of $[CH_3.CH(OH).COO]_2Ca, 5H_2O$.

Preparation.—(1) Calcium lactate is formed as an intermediate product during the manufacture of lactic acid (p. 253).

(2) For pharmaceutical purposes it is prepared by adding the theoretical quantity of calcium carbonate to a hot dilute solution of lactic acid:

$$CaCO_3 + 2CH_3.CH(OH).COOH = [CH_3.CH(OH).COO]_2Ca + CO_2 + H_2O.$$

The hot liquid is filtered and the filtrate evaporated to crystallisation.

Properties.—Colourless crystals, or a white granular powder. When freshly prepared it is slowly soluble 1-18·5 in water, forming a clear, colourless solution, but samples which have been kept for any length of time are less soluble. Slightly soluble in alcohol (90 per cent). The aqueous solution reduces an acid solution of potassium permanganate on warming, an odour of aldehyde being evolved. The salt can be completely dehydrated by heating to 100°. On strong ignition it chars, and yields a residue of calcium carbonate or oxide.

Tests for Impurities. *Absence of Alkali and Limit of Acidity.*—A solution of 5 grammes in hot water does not become pink on the addition of a few drops of phenolphthalein, and requires not more than 5 mils of N/10 sodium hydroxide to produce a pink coloration.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—The calcium can be determined by treating a weighed quantity of the salt in a crucible with concentrated sulphuric acid, igniting, cooling, and repeating the ignition with sulphuric acid until a white residue of calcium sulphate remains, and finally weighing the residue :

$$[CH_3 . CH(OH) . COO]_2Ca \longrightarrow CaSO_4,$$
$$308 = 136,$$
$$1 \text{ gramme } [CH_3 . CH(OH) . COO]_2Ca = 0{\cdot}441 \text{ gramme } CaSO_4.$$

The Pharmacopœia requires that 1 gramme of the salt, treated in this way, shall yield a residue weighing between 0·410 gramme and 0·450 gramme.

Syrupus Calcii Lactophosphatis. *Syrup of Calcium Lactophosphate.*—Concentrated phosphoric acid is added to a suspension of calcium lactate in water, the mixture stirred until solution is complete, orange-flower water added, and then refined sugar, the last ingredient being dissolved without the aid of heat. The volume is adjusted with water and the product filtered.

COMPOUNDS OF STRONTIUM

Sr (Atomic Wt. = 87·5)

Strontium occurs in Nature in the form of its carbonate, *strontianite*, $SrCO_3$, and its sulphate, *celestine*, $SrSO_4$. Only one strontium salt, the bromide, is official.

General Tests for Strontium.—(1) The addition of ammonium chloride and ammonium hydroxide, followed by ammonium carbonate, to a solution of a strontium salt produces a white precipitate of strontium carbonate.

(2) Dilute sulphuric acid, added to a solution of a strontium salt, produces a white precipitate of strontium sulphate. As strontium sulphate is much less soluble than calcium sulphate, it is precipitated when a solution of calcium sulphate is added to a solution of a strontium salt.

(3) A strontium salt, moistened with hydrochloric acid, imparts a bright crimson colour to the bunsen flame.

STRONTII BROMIDUM

Strontium Bromide, $SrBr_2,6H_2O$. (Mol. Wt. = 355·5)

This is required to contain not less than 97 per cent of $SrBr_2,6H_2O$.

Preparation.—(1) Dilute hydrobromic acid is treated with a slight excess of strontium carbonate and the liquid filtered :

$$SrCO_3 + 2HBr = SrBr_2 + CO_2 + H_2O.$$

The filtrate is evaporated until crystals begin to form, cooled, and the crystals are separated and dried carefully at a moderate temperature.

(2) Strontium hydroxide may be employed instead of the carbonate, and the advantage of this method lies in the fact that the hydroxide is more easily obtained in pure form than the carbonate. In this case a slight excess of hydrobromic acid must be employed, because strontium hydroxide is soluble in water, and any excess of it cannot be removed by filtration.

Properties.—Colourless, very deliquescent crystals, with a bitter, saline; metallic taste. Soluble more than 1-1 in water and in alcohol (90 per cent), the solutions being neutral. On heating, the salt melts in its water of crystallisation, and becomes anhydrous at 120° to 130°. The anhydrous salt melts at a red heat without decomposition.

Tests for Impurities. *Barium.*—Dissolve about 1 gramme in water, add sodium acetate, acetic acid, and potassium chromate. There should be no precipitate, even on standing.

Iodide.—According to the B.P.C., when an aqueous solution is mixed with chloroform and dilute chlorine water added, drop by drop, the liberated bromine should dissolve in the chloroform layer to form a brown solution without any violet tinge.

Lead Limit.—20 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—(1) The volumetric estimation is based upon precipitation of the bromide as the silver salt, as described under Potassii Bromidum. Weigh about 2 grammes, dissolve, and dilute to 100 mils. Titrate portions of 20 mils with N/10 silver nitrate, using potassium chromate as indicator:

$$2AgNO_3 + SrBr_2 = 2AgBr + Sr(NO_3)_2,$$
$$2 \times 170 \equiv 355{\cdot}5,$$
$$1000 \text{ mils N/1 } AgNO_3 \equiv 177{\cdot}7 \text{ grammes of } SrBr_2,6H_2O,$$
$$1 \text{ mil N/10 } AgNO_3 \equiv 0{\cdot}01777 \text{ gramme of } SrBr_2,6H_2O.$$

(2) The salt is also estimated gravimetrically, by conversion into sulphate and weighing. Weigh about 0·5 gramme in a crucible, add a little concentrated sulphuric acid, and ignite. Cool in a desiccator and weigh from time to time until the weight is constant:

$$SrBr_2 + H_2SO_4 = SrSO_4 + 2HBr,$$
$$355{\cdot}5 \text{ grammes of } SrBr_2,6H_2O \equiv 183{\cdot}5 \text{ grammes of } SrSO_4.$$

CHAPTER VIII

COMPOUNDS OF MAGNESIUM AND ZINC

COMPOUNDS OF MAGNESIUM

Mg (Atomic Wt. = 24)

In combination, magnesium is widely distributed in Nature, the most important sources being the minerals *dolomite* (p. 98) and *magnesite*, $MgCO_3$. Magnesium is also found in the Stassfurt deposits as *carnallite*, $MgCl_2,KCl,6H_2O$, and as *kieserite*, $MgSO_4,H_2O$; and it is a constituent of many natural silicates, including *talc* (p. 49) and *asbestos*. Magnesium sulphate is found in the waters of many mineral springs.

General Tests for Magnesium.—(1) Ammonium carbonate precipitates from solutions of magnesium salts a basic carbonate of magnesium, but the precipitation is prevented by the presence of ammonium chloride.

(2) Sodium phosphate, added to a solution of a magnesium salt, previously made alkaline with ammonium hydroxide, produces a white precipitate of magnesium ammonium phosphate, $MgNH_4PO_4$. In dilute solutions this may only appear after shaking and allowing to stand.

MAGNESIA PONDEROSA

Heavy Magnesia

Heavy Magnesium Oxide, MgO. (Mol. Wt. = 40)
Syn. Heavy Calcined Magnesia

Preparation.—It is prepared by heating *heavy* magnesium carbonate (*q.v.*) to dull redness until carbon dioxide is no longer evolved:

$$3MgCO_3,Mg(OH)_2,4H_2O = 4MgO + 3CO_2 + 5H_2O.$$

Properties.—It occurs as a fine white powder which slowly absorbs carbon dioxide and moisture from the atmosphere. Very slightly soluble in water, but sufficiently so to form a solution distinctly alkaline to phenolphthalein. Mixed with fifteen times

its weight of water it forms a gelatinous mass on standing for half an hour. On strongly heating, it becomes incandescent. It dissolves in acids with formation of the magnesium salt of the acid used.

Tests for Impurities (to be applied to the solution in dilute hydrochloric acid). *Copper.*—Add excess of ammonium hydroxide, and filter. The filtrate should have no blue tinge and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—The addition of nitric acid, followed by potassium ferrocyanide, should produce not more than the slightest blue or green colour.

Aluminium.—Add nitric acid and then excess of sodium hydroxide. Filter, add to the filtrate ammonium chloride, and boil. No flocculent precipitate should be produced.

Calcium.—Add ammonium chloride and ammonium hydroxide in excess, and then ammonium oxalate solution. There should not be more than a slight precipitate.

Sulphate.—Add barium chloride, when there should not be more than a slight turbidity.

Carbonate.—According to the B.P.C., if 0·1 gramme of the substance be heated to boiling with 5 mils of water, cooled and poured into an equal volume of acetic acid, it should dissolve, and show not more than a few isolated gas bubbles.

Lead Limit.—20 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Test. *Limit of Carbon Dioxide and Moisture.*—It should lose not more than 1 per cent of its weight when heated to dull redness. Weigh about 1 gramme in a crucible, and ignite. Cool in a desiccator and then weigh, repeating the ignition, cooling, and weighing until the weight is constant.

MAGNESIA LEVIS

Light Magnesia

Light Magnesium Oxide, MgO. (Mol. Wt. = 40.)
Syn. Light Calcined Magnesia

Preparation.—This is prepared by heating *light* magnesium carbonate (*q.v.*) to dull redness, until carbon dioxide is no longer evolved :

$$3MgCO_3,Mg(OH)_2,3H_2O = 4MgO + 3CO_2 + 4H_2O.$$

Properties.—A very light, white powder, differing from Magnesia Ponderosa in bulk only, the volumes which correspond to the same weight having the ratio of 3·5 to 1.

Tests for Impurities.—Test as described under Magnesia Ponderosa.

Quantitative Test.—As for Magnesia Ponderosa, but employing 0·5 gramme.

MAGNESII CARBONAS PONDEROSUS

Heavy Magnesium Carbonate

This is a hydrated basic carbonate of magnesium, having the approximate formula $3MgCO_3,Mg(OH)_2,4H_2O$.

Preparation.—The pharmacopœial method of preparation consists in dissolving 125 parts of magnesium sulphate and 150 parts of sodium carbonate separately, each in 250 parts of *boiling* water. The solutions are mixed, evaporated to dryness, and the residue of heavy magnesium carbonate and sodium sulphate digested with 500 parts of boiling water for half an hour. The liquid is filtered through a calico filter, the insoluble carbonate being washed on the filter until free from sulphate, and then dried in a water oven. The reactions may be represented by the equations :

$$Na_2CO_3 + MgSO_4 = MgCO_3 + Na_2SO_4,$$
$$4MgCO_3 + 5H_2O = 3MgCO_3,Mg(OH)_2,4H_2O + CO_2.$$

Properties.—A white, granular powder, insoluble in water. It dissolves readily in dilute acids with effervescence and formation of the magnesium salt of the acid used. When heated to redness it loses carbon dioxide and water, leaving a residue of magnesium oxide.

Tests for Impurities. *Copper, Aluminium, and Iron.*—Test as described under Magnesia Ponderosa.

Calcium.—There should be no indication of this when tested as under Magnesia Ponderosa.

Chloride.—A solution in dilute nitric acid should give not more than a faint opalescence on the addition of silver nitrate.

Sulphate.—Test as under Magnesia Ponderosa.

Lead Limit.—20 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Test.—When about 1 gramme is heated to redness in the manner described under Magnesia Ponderosa, it should lose between 56 and 58 per cent of its weight.

MAGNESII CARBONAS LEVIS

Light Magnesium Carbonate

This is a hydrated basic carbonate of magnesium having the approximate formula $3MgCO_3,Mg(OH)_2,3H_2O$.

Preparation.—The pharmacopœial method of preparation consists in dissolving 125 parts of magnesium sulphate and 150 parts

of sodium carbonate separately, each in 1000 parts of *cold* water, mixing the solutions, and heating to boiling. After boiling for fifteen minutes the precipitate is collected on a calico filter, washed free from sulphate, and dried in a water oven.

It should be noted that the difference between the conditions of the formation of the light and heavy magnesium carbonates consists essentially in the concentration of the reacting solutions, the temperature at which they are mixed, and the subsequent treatment of the precipitate.

Properties.—A very light, white powder, which under the microscope is seen to consist of amorphous particles mixed with slender prisms. In other properties it resembles Magnesii Carbonas Ponderosus.

Tests for Impurities.—As described under Magnesii Carbonas Ponderosus.

Quantitative Test.—When 0·5 gramme is heated as described under Magnesia Ponderosa it should lose between 56 and 58 per cent of its weight (B.P.C.).

LIQUOR MAGNESII BICARBONATIS

Solution of Magnesium Bicarbonate. *Syn.* Fluid Magnesia

Preparation.—Basic magnesium carbonate is freshly precipitated by mixing a solution of sodium carbonate with a boiling solution of magnesium sulphate :

$$MgSO_4 + Na_2CO_3 = MgCO_3 + Na_2SO_4,$$
$$4MgCO_3 + H_2O = 3MgCO_3,Mg(OH)_2 + CO_2.$$

The liquid is boiled until evolution of carbon dioxide ceases, the precipitate collected on a calico filter, and washed free from sulphate. The washed precipitate is suspended in water and introduced into a suitable aerating apparatus. Pure, washed carbon dioxide is then led in, and the mixture allowed to remain in contact with excess of the gas for twenty-four hours or more at a pressure of about three atmospheres, the following reaction taking place with production of soluble magnesium bicarbonate :

$$3MgCO_3,Mg(OH)_2 + 5CO_2 + 3H_2O = 4Mg(HCO_3)_2.$$

The solution is decanted and again saturated with carbon dioxide before being transferred to securely closed bottles.

Properties.—A colourless solution which may effervesce slightly when the containing bottle is first opened. On keeping, a deposition of basic carbonate of magnesium occurs with loss of carbon dioxide, the solution suffering a corresponding decrease in strength ; for this reason it should only be used when comparatively fresh. When evaporated to dryness a residue is obtained, which dissolves in dilute acids with effervescence, the resulting solution yielding the reactions characteristic of magnesium.

Tests for Impurities. *Sulphate.*—The addition of excess of dilute hydrochloric acid, followed by boiling, should produce a solution which yields no precipitate with barium chloride.

Lead Limit.—0·5 part per million (p. 173).

Arsenic Limit.—0·2 part per million (p. 176).

Quantitative Test.—The residue obtained by evaporating 20 mils of the solution to dryness should, after ignition, weigh not less than 0·16 and not more than 0·19 gramme. This corresponds to approximately 2 per cent *w/v* of the official magnesium carbonate.

MAGNESII SULPHAS

Magnesium Sulphate, $MgSO_4,7H_2O$. (Mol. Wt. = 246.)
Syn. Epsom Salts

This is required to contain not less than 97·4 per cent of $MgSO_4,7H_2O$.

Preparation.—(1) It may be prepared by acting upon magnesium, or its oxide or carbonate, with dilute sulphuric acid and evaporating the resulting solution to crystallisation :

$$Mg + H_2SO_4 = MgSO_4 + H_2,$$
$$MgO + H_2SO_4 = MgSO_4 + H_2O,$$
$$3MgCO_3Mg(OH)_2,4H_2O + 4H_2SO_4 = 4MgSO_4 + 3CO_2 + 9H_2O.$$

(2) It can be prepared from magnesite (p. 109) by the action of dilute sulphuric acid :

$$MgCO_3 + H_2SO_4 = MgSO_4 + H_2O + CO_2.$$

(3) It is manufactured by the action of dilute sulphuric acid on previously powdered and calcined dolomite (p. 98). This results in the formation of readily soluble magnesium sulphate and the deposition of the sparingly soluble calcium sulphate. The liquid is filtered and the filtrate concentrated to crystallisation.

(4) Magnesium sulphate is also largely manufactured from the native sulphate kieserite, $MgSO_4,H_2O$, which is almost insoluble in water, but which, on keeping in contact with water, slowly dissolves to form a solution of $MgSO_4,7H_2O$.

Properties.—Small, colourless, prismatic needles or rhombic prisms with a cooling, saline, and rather bitter taste. Soluble 1-1 in water, the solution being neutral to litmus. On heating to 150°-160° for some time, it loses 6 molecules of water, the remaining monohydrated salt becoming completely anhydrous at about 280°.

Tests for Impurities. *Insoluble Impurities and more than Traces of Iron.*—10 grammes, dissolved in 20 mils of water and heated on a water-bath for one hour in a closed flask, should yield a clear, colourless solution.

Zinc.—Add ammonium chloride and hydroxide to the aqueous solution, filter if necessary, and add ammonium sulphide, when there should be no precipitate.

Chloride.—Acidify the aqueous solution with nitric acid, and add silver nitrate. There should not be more than a slight opalescence.

Lead Limit.—5 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—The magnesium in the salt is estimated gravimetrically by precipitation as magnesium ammonium phosphate, $MgNH_4PO_4,6H_2O$, and conversion of the precipitate into magnesium pyrophosphate, $Mg_2P_2O_7$, by ignition.

Weigh about 0·5 gramme of the salt, dissolve in 50 mils of water, and add successively to the solution 20 mils of strong ammonium hydroxide, and excess of sodium phosphate solution. Stir the mixture well and allow to stand for two or three hours. Collect the precipitate on a filter paper, wash well with dilute ammonia, and dry in a water-oven. Separate the precipitate from the filter paper as far as possible, carrying out the operation over a sheet of black, glazed paper in order that none may be lost. Ignite the filter paper in a weighed crucible, and, when the ash is quite white, allow to cool, and add the precipitate. Again heat, gently at first, and finally to redness; cool in a desiccator and weigh; continue to ignite and weigh until the weight is constant:

$$MgSO_4 + Na_2HPO_4 + NH_4OH + 5H_2O = MgNH_4PO_4,6H_2O + Na_2SO_4,$$
$$2MgNH_4PO_4,6H_2O = Mg_2P_2O_7 + 2NH_3 + 13H_2O,$$
$$Mg_2P_2O_7 \equiv 2MgSO_4,7H_2O.$$
$$222 \simeq 2 \times 246.$$

The Pharmacopœia requires that 0·5 gramme of Magnesii Sulphas, treated as described above, shall yield a residue weighing between 0·220 and 0·226 gramme.

Magnesii Sulphas Effervescens. *Effervescent Magnesium Sulphate. Syn.* Effervescent Epsom Salts.—Magnesium sulphate, dried until it has lost 23 per cent of its weight and powdered, is mixed with tartaric acid, citric acid, sodium bicarbonate, and refined sugar on a water-bath, the resulting pasty mass being forced through a sieve to produce granules of uniform size, which are dried at a temperature not exceeding 55° (cf. Sodii Phosphas Effervescens, p. 79).

COMPOUNDS OF ZINC

Zn (Atomic Wt. = 65·5)

The principal zinc ores are *calamine*, $ZnCO_3$, and *zinc blende*, ZnS. The compounds of zinc used in pharmacy are all prepared directly or indirectly from the metal, and it is therefore necessary to describe briefly the chief method employed for the production of the metal from its ores.

The first process consists in roasting the ore in air, when zinc

oxide is obtained, whether the ore employed be calamine or zinc blende :

$$ZnCO_3 = ZnO + CO_2,$$
$$2ZnS + 3O_2 = 2ZnO + 2SO_2.$$

The oxide is then mixed with coke and strongly heated in earthenware retorts, when metallic zinc distils :

$$ZnO + C = Zn + CO.$$

Commercial zinc, prepared in this way, contains traces of other metals, particularly iron, lead, cadmium, and manganese, which are present in small quantities in most zinc ores.

General Tests for Zinc.—(1) Heated on charcoal with fusion mixture, zinc compounds give an incrustation of zinc oxide, which appears yellow when hot, but becomes white again on cooling. If the incrustation be moistened with cobalt nitrate and reheated, it yields a green mass.

(2) Ammonium hydroxide precipitates from solutions of zinc salts a white precipitate of zinc hydroxide, $Zn(OH)_2$, readily soluble in excess of the reagent with formation of an ammine of the type $Zn(NH_3)_4SO_4$. The precipitation is completely prevented by the presence of ammonium chloride.

Sodium hydroxide also precipitates zinc hydroxide from solutions of its salts, but the precipitate is readily soluble in excess of the reagent with formation of sodium zincate, $NaZnO_2$.

(3) Add to a solution of a zinc salt ammonium chloride and hydroxide, followed by ammonium sulphide. A white precipitate of zinc sulphide is produced, easily soluble in dilute mineral acids.

ZINCI OXIDUM

Zinc Oxide, ZnO. (Mol. Wt. = 81·5).

Preparation.—(1) The oxide remains when basic zinc carbonate is ignited in a crucible. The ignition is continued until a portion tested with a dilute acid no longer effervesces :

$$ZnCO_3,2Zn(OH)_2,H_2O = 3ZnO + CO_2 + 3H_2O.$$

Too high a temperature should not be employed or the product may be discoloured.

(2) The oxide is manufactured by heating metallic zinc to bright redness in contact with air. The vapour of the metal burns to form the oxide, which is collected as a fine white powder.

Properties.—A very fine, white or yellowish-white, amorphous impalpable powder, free from gritty particles, and odourless. Insoluble in water, but soluble in dilute acids with production of the salt of the acid used; soluble in ammonium hydroxide, the solution usually being somewhat opalescent. On keeping, it slowly

absorbs moisture and carbon dioxide from the air with formation of the carbonate. When heated, it becomes pale yellow, but becomes white again on cooling. Heated with carbon it is reduced to metallic zinc; heated with magnesium it is reduced with considerable violence.

Tests for Impurities.—To be applied to a solution in dilute hydrochloric acid except where otherwise stated.

Copper, Cadmium, and Lead.—Dilute and pass hydrogen sulphide. If a precipitate be produced, examine by Table on p. 423. Copper and cadmium should be completely absent, and there should not be more than the slightest reactions for lead.

Iron.—Add nitric acid and potassium ferrocyanide, when there should be no blue or green colour.

Aluminium.—Add nitric acid, followed by excess of sodium hydroxide. Dilute, filter off any precipitate, then add excess of ammonium chloride to the filtrate and boil, when there should be no precipitate.

Manganese (Limit of).—To a solution of 0·2 gramme in dilute sulphuric acid add excess of ammonium hydroxide, filter off any precipitate; dissolve this in dilute nitric acid, dilute to 15 mils, boil, and add 1 mil of N/10 silver nitrate solution and 10 mils of 1-10 ammonium persulphate solution, when there should be no more than a faint pink coloration.

Before testing for the remaining impurities, remove the zinc by adding ammonium chloride, ammonium hydroxide, and ammonium sulphide, and filtering off the precipitate of zinc sulphide.

Calcium.—Add excess of ammonium hydroxide and ammonium oxalate. There should be no white precipitate.

Magnesium.—Add excess of ammonium hydroxide and sodium phosphate. There should be no precipitate even on shaking and allowing to stand.

Sodium and Potassium.—Apply the flame test to the oxide moistened with hydrochloric acid, using an indigo prism to detect the potassium if sodium be present.

Ammonium.—Boil with excess of sodium hydroxide solution, and test the evolved vapours with turmeric paper (p. 32).

Carbonate.—The dry substance should dissolve without effervescence in dilute acids.

Limit of Alkali.—The B.P.C. states that 1 gramme, treated with 10 mils of boiling water and 0·1 mil of phenolphthalein solution, should require not more than 1 mil of N/10 hydrochloric acid to discharge the red colour.

Carbon.—The substance should dissolve in dilute hydrochloric acid without the separation of any black particles.

Arsenic Limit.—10 parts per million (p. 176).

ZINCI CARBONAS

Zinc Carbonate

This is a basic carbonate of zinc of the approximate composition $ZnCO_3,2Zn(OH)_2,H_2O$.

Preparation.—The B.P.C. gives the following method: A solution of 30 parts of zinc sulphate in 150 parts of water is added, with constant stirring, to a filtered, boiling solution of 32 parts of sodium carbonate in 180 parts of water. After boiling for fifteen minutes, the precipitate is allowed to subside. The liquid is decanted, and the precipitate is washed with hot water until free from chloride, collected, pressed, and dried at 50°. Under different conditions of preparation the product is liable to variation.

Properties.—A white, amorphous, impalpable powder, insoluble in water. When strongly heated it is converted into zinc oxide, with loss of carbon dioxide and water.

Tests for Impurities. *Copper, Cadmium, Lead, Iron, Aluminium, Calcium, Magnesium, Sodium, Potassium, and Ammonium.*—Test as under Zinci Oxidum. Lead should be completely absent.

Manganese (Limit of).—Test as under Zinci Oxidum.

Chloride.—Dissolve in dilute nitric acid and test with silver nitrate, when there should not be more than a faint opalescence.

Sulphate.—Dissolve in dilute hydrochloric acid and add barium chloride. There should not be more than a slight turbidity.

Arsenic Limit.—10 parts per million (p. 176).

ZINCI CHLORIDUM

Zinc Chloride, $ZnCl_2$. (Mol. Wt. = 136·5.)

Preparation.—This is prepared by dissolving zinc in hydrochloric acid and evaporating to dryness:

$$Zn + 2HCl = ZnCl_2 + H_2.$$

The residue is heated to fusion and poured into cylindrical moulds or trays to solidify, the solid substance being transferred while still hot to warmed, dried, well-stoppered bottles.

Iron and lead, which are common impurities in commercial zinc, must, if present, be removed before evaporation by the method described below under Liquor Zinci Chloridi.

Properties.—Usually in the form of opaque, porcelain-like sticks or irregular fragments, or a granular powder. Very deliquescent and caustic. Soluble 10·4 in water, 1·1 in alcohol (90 per cent). The aqueous solution is acid to litmus owing to hydrolysis, and on evaporation is partly decomposed, forming zinc oxychloride. The solution has an astringent metallic taste.

Tests for Impurities. *Metallic Impurities and Ammonium.*—Test as described under Zinci Oxidum, except that no trace of lead is permitted.

Manganese (*Limit of*).—0·25 gramme, dissolved in water and tested as under Zinci Oxidum, should yield a solution having not more than a faint pink coloration.

Sulphate.—Dissolve in dilute hydrochloric acid and add barium chloride. There should be no turbidity.

Oxychloride (*Limit of*).—The B.P.C. prescribes the following test: A 5 per cent solution should be clear, or only very slightly opalescent; and if it be mixed with an equal volume of alcohol a single drop of hydrochloric acid should suffice to render 10 mils of the mixture perfectly clear.

Arsenic Limit.—5 parts per million (p. 176).

LIQUOR ZINCI CHLORIDI

Solution of Zinc Chloride

Preparation.—Granulated zinc (40 parts) is added to a mixture of hydrochloric acid (110 parts) and water (50 parts) contained in a porcelain dish, and the mixture heated until hydrogen is no longer evolved. The resulting solution of zinc chloride is boiled for half an hour to expel dissolved gases, the water lost by evaporation is replaced, and the solution allowed to cool.

The next step is to free the solution from traces of iron or lead which commonly accompany commercial zinc, and which the solution may now contain as chlorides. If a small portion on testing shows the presence of these impurities, sufficient chlorine water is added to the whole to bring about the oxidation of ferrous chloride to the ferric state. The addition of zinc carbonate now results in the precipitation of all the iron and lead as carbonate, and neutralises the excess of acid, while zinc chloride, which is the other product of the reaction, remains in solution. It should be noted that, were the usual precipitant, ammonium hydroxide, employed, an impurity would be introduced in the form of ammonium chloride.

The solution is filtered, and the filtrate evaporated to 100 parts by volume. During evaporation, any excess of chlorine is expelled.

Properties.—A colourless liquid with an astringent and sweetish taste. Specific gravity, 1·530. It is more suitable for use in astringent lotions than solid zinc chloride owing to the fact that it is free from zinc oxychloride (p. 117). It is a powerful disinfectant, of which the properties are not destroyed by contact with organic matter.

Tests for Impurities. *Copper, Cadmium, Lead, Iron, Aluminium, Calcium, and Magnesium.*—There should be no indication of these on testing as under Zinci Oxidum.

Arsenic.—There should be no indication on applying Fleitmann's test (p. 143).

Sulphate.—There should be no turbidity on the addition of barium chloride.

ZINCI SULPHAS

Zinc Sulphate, $ZnSO_4,7H_2O$. (Mol. Wt. = 287·5.)
Unofficial Syn. White Vitriol

Preparation.—(1) In the laboratory this salt may be prepared by adding excess of zinc to dilute sulphuric acid :

$$Zn + H_2SO_4 = ZnSO_4 + H_2.$$

When effervescence has ceased, the solution is filtered and evaporated to crystallisation.

(2) It is manufactured by roasting zinc blende (p. 114) in air at a low temperature, the product being allowed to cool, and then extracted with water :

$$ZnS + 2O_2 = ZnSO_4.$$

Properties.—Colourless, transparent, somewhat efflorescent prisms, with a metallic, astringent taste. Soluble more than 1-1 in water, the solution being acid to litmus owing to hydrolysis; insoluble in alcohol (90 per cent). On heating, it loses five molecules of water at 50° without melting. Another molecule is lost at 100°; and at about 250° the salt partially decomposes with loss of the last molecule of water and some sulphuric acid.

Tests for Impurities. *Copper, Cadmium, Lead, Iron, Aluminium, Calcium, Magnesium, Sodium, Potassium, and Ammonium.*—Test as under Zinci Oxidum. A trace of iron is permitted, but lead should be completely absent.

Manganese (Limit of).—0·5 gramme, dissolved in water and tested as under Zinci Oxidum, should yield a solution having not more than a faint pink coloration.

Chloride.—Add to an aqueous solution nitric acid and silver nitrate, when there should not be more than a slight turbidity.

Acetate.—Gently warm the salt with concentrated sulphuric acid, when there should be no odour of acetic acid.

Arsenic Limit.—5 parts per million (p. 176).

ZINCI ACETAS

Zinc Acetate, $(CH_3.COO)_2Zn,2H_2O$. (Mol. Wt. = 219·5)

Preparation.—Hot dilute acetic acid is neutralised with zinc oxide or carbonate and the liquid filtered, then evaporated to crystallisation :

$$2CH_3.COOH + ZnO = (CH_3.COO)_2Zn + H_2O,$$
$$2CH_3.COOH + ZnCO_3 = (CH_3.COO)_2Zn + CO_2 + H_2O.$$

The crystals are collected and dried at ordinary temperatures on porous plates or between sheets of filter paper.

Properties.—Thin, translucent, colourless, crystalline plates

with a pearly lustre. The crystals have a faint odour of acetic acid and a sharp, metallic taste. Soluble 1-2·5 in water, forming an acid solution owing to hydrolysis. On long exposure to air, the salt effloresces and is partly converted into a basic salt with loss of acetic acid. For this reason, samples that have been exposed to air may not form a clear solution in water, and the salt should, therefore, be kept in well-stoppered bottles. When gently heated, the crystals partially melt with loss of water of crystallisation. At higher temperatures the salt decomposes with evolution of acetone and other inflammable vapours, leaving a residue of zinc oxide.

Tests for Impurities. *Copper, Cadmium, Lead, Iron, Aluminium, Calcium, Magnesium, Sodium, Potassium, and Ammonium.*—Test as under Zinci Oxidum. Lead should be completely absent.

Manganese (Limit of).—0·5 gramme, dissolved in water and tested as under Zinci Oxidum, should yield a solution having not more than a faint pink coloration.

Sulphate.—The aqueous solution, acidified with dilute hydrochloric acid, should yield no turbidity on the addition of barium chloride.

Chloride.—The aqueous solution, acidified with dilute nitric acid, should yield no opalescence with silver nitrate.

Arsenic Limit.—5 parts per million (p. 176).

ZINCI VALERIANAS

Zinc Valerianate, $(C_4H_9.COO)_2Zn,2H_2O$. (Mol. Wt. = 303·5.)
Unofficial Syn. Zinc Valerate

This is a mixture of the zinc salts of iso-valerianic acid, $\begin{matrix}CH_3\\CH_3\end{matrix}\!>\!CH.CH_2.COOH$, and optically active valerianic acid, $\begin{matrix}CH_3\\CH_3.CH_2\end{matrix}\!>\!CH.COOH$ (p. 252).

Preparation.—(1) It may be prepared by neutralising commercial iso-valerianic acid with zinc carbonate:

$$2C_4H_9.COOH + ZnCO_3 = (C_4H_9.COO)_2Zn + CO_2 + H_2O.$$

(2) It is generally manufactured by mixing solutions of zinc sulphate and the sodium salt of iso-valerianic acid, at a temperature not exceeding 70°:

$$2C_4H_9.COONa + ZnSO_4 = (C_4H_9.COO)_2Zn + Na_2SO_4.$$

The precipitated zinc valerianate is separated, washed with a little water, and dried on a porous plate at ordinary temperatures.

Properties.—White, lustrous scales, or a white powder, having the disagreeable odour of valerianic acid. Variations in the method of preparation may result in a salt containing less than two molecules of water of crystallisation. Very slightly soluble in cold water:

soluble in hot water and in alcohol (90 per cent). On boiling the aqueous solution a slight turbidity is produced, due to loss of valerianic acid and formation of a basic salt. When heated, the salt melts, and then decomposes, evolving inflammable vapours, and finally leaving a residue of zinc oxide.

Tests for Impurities.—Before testing for metallic impurities the salt must be ignited, the residue extracted with hydrochloric acid, and the liquid filtered.

Copper, Cadmium, Lead, Iron, Aluminium, Calcium, Magnesium, Sodium, Potassium, and Ammonium.—Test as under Zinci Oxidum.

Manganese (Limit of).—0·2 gramme of the zinc oxide obtained by ignition of the salt, when tested as described under Zinci Oxidum, should yield a solution having not more than a faint pink coloration.

Carbonate.—The dry salt should not effervesce on treatment with dilute acids.

Chloride and Sulphate.—Shake the salt with dilute nitric acid and filter through a wet filter-paper to remove the liberated valerianic acid. Separate portions of the filtrate should not give more than the slightest turbidity with barium chloride, nor more than the slightest opalescence with silver nitrate.

Acetate.—Triturate 0·5 gramme of the salt with 3 mils of water, add a few drops of ferric chloride, and filter. The filtrate should have no red colour.

Butyrate.—The Pharmacopœia states that when heated in a retort with dilute sulphuric acid it yields a distillate which, when added to copper acetate solution, should not immediately become turbid or opalescent (owing to precipitation of copper butyrate), but forms after a time oily drops, which gradually pass into a bluish-white crystalline deposit.

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—The zinc in this salt is estimated gravimetrically by conversion into oxide, ZnO. About 0·5 gramme is weighed in a crucible, ignited, cooled, moistened with a little concentrated nitric acid, ignited again, and weighed :

$$(C_4H_9 . COO)_2Zn,2H_2O \equiv ZnO,$$
$$303{\cdot}5 \text{ grammes} \equiv 81{\cdot}5 \text{ grammes.}$$

The Pharmacopœia requires that zinc valerianate, treated in this way, shall yield between 26 and 27 per cent of zinc oxide.

CHAPTER IX

COMPOUNDS OF IRON, ALUMINIUM, AND CHROMIUM

IRON AND ITS COMPOUNDS

Fe (Atomic Wt. = 56)

IRON is one of the most commonly occurring metals. It is not generally met with in the free state, but its ores are widely distributed in Nature, and include *red hæmatite*, Fe_2O_3, *brown hæmatite*, $2Fe_2O_3,3H_2O$, *magnetic iron ore*, Fe_3O_4, *spathic iron ore*, $FeCO_3$, *iron pyrites*, FeS_2, and *copper pyrites*, CuS,Fe_2S_3.

Iron forms two series of salts—the *ferrous* salts, derived from ferrous oxide, FeO, and the *ferric* salts, derived from ferric oxide, Fe_2O_3. The ferrous salts, on exposure to air, usually become slowly oxidised to ferric salts.

Extraction.—Iron is generally manufactured from red or brown hæmatite. The previously calcined ore is smelted in a blast furnace with coke and limestone, whereupon the carbon of the coke is oxidised by the air blast to carbon monoxide, and this reduces the iron oxide to the metal:

$$Fe_2O_3 + 3CO = 2Fe + 3CO_2.$$

The limestone combines with the siliceous matter present in the ore to produce a fusible slag, which forms the upper layer of a molten mass that collects at the bottom of the furnace. The lower layer of the mass consists of molten iron, and this is run off at intervals into moulds of sand, the product being known as pig iron or cast iron.

The chemical changes that occur in the blast furnace are complex and too technical to be considered here. Pig iron is very impure, containing from 2 to 6 per cent of carbon, together with varying quantities of manganese, silicon, sulphur, and phosphorus, and is converted by various methods into steel or wrought iron.

Wrought iron is the purest commercial form of iron, and is prepared from pig or cast iron by melting in a reverberatory furnace lined with ferric oxide, when most of the impurities in the iron become oxidised, the carbon escaping as carbon dioxide and the remaining impurities combining with the ferric oxide to form a slag. During this process the mass of iron becomes "pasty", owing to

the fact that wrought iron melts at a higher temperature than pig iron. The product is removed from the furnace in large lumps and freed from slag under the steam-hammer.

Wrought iron, unlike cast iron, is both malleable and ductile, and can be formed into wire, sheets, nails, etc.

General Tests for Iron.—(1) Solutions of ferric salts yield a dark blue precipitate (Prussian blue) with potassium ferrocyanide solution :

$$4FeCl_3 + 3K_4Fe(CN)_6 = 12KCl + Fe_4[Fe(CN)_6]_3.$$

Ferrous salts yield this blue precipitate only after oxidation to the ferric state, this being done usually by warming with nitric acid. But ferrous salts do yield with potassium ferrocyanide a white to greenish-blue precipitate, gradually becoming darker in colour owing to oxidation.

(2) Ferric salts yield with potassium thiocyanate a wine-red coloration, due to the production of soluble ferric thiocyanate :

$$FeCl_3 + 3KSCN = 3KCl + Fe(SCN)_3.$$

Ferrous salts only yield this coloration after oxidation.

(3) Ferric salts give a reddish - brown precipitate of ferric hydroxide on the addition of ammonium hydroxide or sodium hydroxide :

$$FeCl_3 + 3NH_4OH = Fe(OH)_3 + 3NH_4Cl.$$

Ferrous salts yield a green precipitate of ferrous hydroxide with these reagents, and, since precipitation is incomplete, it is necessary to oxidise the salt to the ferric state by means of nitric acid before attempting to remove the iron from a solution by this method.

(4) Ferrous salts give a dark blue precipitate (Turnbull's blue) with potassium ferricyanide (p. 306).

(5) Ammonium sulphide produces with ferric or ferrous salts in neutral or alkaline solution a black precipitate of ferrous sulphide, FeS.

FERRUM

Iron

Iron of the Pharmacopœia is annealed wrought iron wire having a diameter of about 0·1 mm. (about No. 35 wire gauge), or wrought iron nails. Both of these should be free from any coating of oxide.

It usually consists of about 99·5 per cent of metallic iron, with only minute traces of carbon, silicon, sulphur, phosphorus, and arsenic. Specific gravity, 7·6 to 8·14.

Arsenic Limit—200 parts per million (p. 176).

FERRUM REDACTUM

Reduced Iron

This is required to contain not less than 80 per cent of Fe, with a variable amount of iron oxide.

Preparation.—Reduced iron is prepared by the reduction of ferric oxide or hydroxide with hydrogen :

$$Fe_2O_3 + 3H_2 = 2Fe + 3H_2O.$$

Ferric hydroxide is freshly precipitated by adding excess of ammonium hydroxide to ferric chloride solution, and the precipitate collected and dried. The hydroxide is introduced into a wrought iron tube, through which is passed a stream of hydrogen, previously dried by means of calcium chloride, the tube being maintained at a dull red heat in a furnace throughout the period of the reaction. When reduction is complete, the tube is allowed to cool and the reduced iron withdrawn, to be transferred to a dry, well-stoppered bottle.

Properties.—A fine, greyish-black powder, which is strongly attracted by a magnet, and produces metallic streaks when rubbed in a mortar. It dissolves in hydrochloric acid with evolution of hydrogen and formation of ferrous chloride.

Tests for Impurities. *Limit of Insoluble Matter.*—Not more than 1 per cent should be insoluble in hydrochloric acid.

Sulphide.—The gas evolved on treatment with hydrochloric acid should have no odour of hydrogen sulphide, and should not darken lead acetate paper.

Arsenic Limit.—200 parts per million (p. 176).

Quantitative Estimation.—The pharmacopœial method of estimation is of considerable interest, and provides a simple method for determining the metallic iron in the sample, exclusive of any oxide that may be present. The method depends upon the fact that metallic iron is able to displace copper from copper sulphate solution. Weigh about 0·25 gramme of the powder and add to a hot solution of 1·25 grammes of copper sulphate in about 20 mils of water contained in a small flask. Heat the mixture for about ten minutes, shaking occasionally. Filter as rapidly as possible from the precipitated copper, avoiding undue exposure to air, rinse the flask with a small quantity of water, and pour this over the filter. Acidify the mixed filtrate and washings with dilute sulphuric acid, and titrate with N/10 potassium permanganate solution :

$$Fe + CuSO_4 = FeSO_4 + Cu,$$

$$2KMnO_4 + 10FeSO_4 + 8H_2SO_4 = 5Fe_2(SO_4)_3 + 2MnSO_4 + K_2SO_4 + 8H_2O,$$

$$2KMnO_4 \equiv 10FeSO_4 \equiv 10Fe,$$

$$316 \equiv 10 \times 56 \text{ of Fe},$$

$$1000 \text{ mils of N/1 } KMnO_4 \equiv 56 \text{ grammes of Fe},$$

$$1 \text{ mil N/10 } KMnO_4 \equiv 0{\cdot}0056 \text{ gramme of Fe}.$$

FERRI SULPHAS

Ferrous Sulphate, $FeSO_4,7H_2O$. (Mol. Wt. = 278)

This is required to contain not less than 97·5 per cent of $FeSO_4,7H_2O$.

Preparation.—It is prepared by adding excess of iron to dilute sulphuric acid, and, on the cessation of effervescence, concentrating by boiling, and then filtering from the undissolved iron :

$$Fe + H_2SO_4 = FeSO_4 + H_2.$$

The filtrate is allowed to cool, and the resulting crystals dried on porous plates.

Properties.—Pale green, rhombic prisms, with an astringent taste. Soluble more than 1-2 in previously boiled and cooled water, forming a solution which is acid, owing to hydrolysis ; insoluble in alcohol (90 per cent). When a strong aqueous solution is poured into alcohol, the salt is precipitated in very small crystals, known commercially as "granulated" ferrous sulphate. Crystals of ferrous sulphate effloresce in dry air, and on exposure to moist air slowly oxidise, becoming coated with a brown, basic ferric sulphate. When heated, ferrous sulphate loses 6 molecules of water at 100° ; and on strong ignition, it evolves water and oxides of sulphur, leaving a residue of ferric oxide :

$$2FeSO_4,H_2O = Fe_2O_3 + SO_3 + SO_2 + 2H_2O.$$

Tests for Impurities. *Copper.*—Boil an aqueous solution with excess of nitric acid to oxidise the salt to the ferric state ; cool, add excess of ammonium hydroxide, and filter. The filtrate should have no blue tinge and should give no brown colour on acidifying with acetic acid and adding a few drops of potassium ferrocyanide.

Zinc.—Boil with nitric acid, add excess of ammonium chloride and ammonium hydroxide, filter off the precipitated ferric hydroxide, and add ammonium sulphide to the filtrate, when there should be no precipitate.

Basic Ferric Sulphate.—When dissolved in 2 parts of previously boiled and cooled water, the solution should be perfectly clear.

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—The salt is estimated by oxidation to ferric sulphate, using standard potassium permanganate in presence of dilute sulphuric acid. Weigh about 3 grammes, dissolve in about 50 mils of dilute sulphuric acid, and dilute to 100 mils. Titrate portions of 20 mils with N/10 potassium permanganate solution :

$$2KMnO_4 + 10FeSO_4 + 8H_2SO_4 = K_2SO_4 + 2MnSO_4 + 5Fe_2(SO_4)_3 + 8H_2O$$

$$2KMnO_4 \equiv 10FeSO_4,7H_2O,$$

$$316 \equiv 10 \times 278,$$

$$1000 \text{ mils N/1 } KMnO_4 \equiv 278 \text{ grammes of } FeSO_4,7H_2O,$$

$$1 \text{ mil N/10 } KMnO_4 \equiv 0{\cdot}0278 \text{ gramme of } FeSO_4,7H_2O.$$

Ferri Sulphas Exsiccatus. *Exsiccated Ferrous Sulphate.*—This substance consists of ferrous sulphate deprived of part of its water of crystallisation. It is required to contain not less than 77 per cent of $FeSO_4$.

Preparation.—Crystallised ferrous sulphate is heated on a water-bath, with constant stirring, until it has lost the requisite amount of water.

Properties.—A greyish-white powder, slowly but completely soluble in water. In other respects it resembles crystalline ferrous sulphate. When used in dispensing, 8 parts of the exsiccated salt may be accepted as the equivalent of 13 parts of the crystalline salt.

It should be free from the impurities mentioned under Ferri Sulphas.

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—It is estimated as described under Ferri Sulphas, employing about 2 grammes of the salt.

LIQUOR FERRI PERCHLORIDI FORTIS

Strong Solution of Ferric Chloride

Ferric chloride is a very hygroscopic solid which is not suitable for pharmaceutical purposes in its ordinary state, and which, on solution in water, gives rise to basic salts by hydrolysis. For these reasons it is only included in the Pharmacopœia in the form of a specially prepared acid solution of definite strength.

Preparation.—It is prepared by dissolving iron in hydrochloric acid and oxidising the resulting ferrous chloride to the ferric state by means of nitric acid. Iron (70 parts) is treated with a mixture of concentrated hydrochloric acid (250 parts) and water (140 parts) and heated in a flask on a wire gauze until effervescence has ceased. The liquid is then boiled to expel all gases, filtered from the undissolved iron, and the flask and filter washed with water to obtain the whole of the ferrous chloride. To the mixed filtrate and washings is added concentrated hydrochloric acid (140 parts) and the solution poured in a slow, continuous stream into concentrated nitric acid (30 parts), oxidation being promoted, if necessary, by gently warming. The resulting solution is then concentrated by evaporation until a precipitate of basic ferric chloride commences to form. This is redissolved by the addition of concentrated hydrochloric acid (20 parts), and then the product is diluted to 350 parts or to the proper specific gravity.

The reactions may be explained as follows. When excess of iron is treated with hydrochloric acid, a solution of ferrous chloride is obtained and hydrogen evolved:

$$Fe + 2HCl = FeCl_2 + H_2.$$

More hydrochloric acid is then added to the filtered liquid in order

to provide the chlorine ions necessary for the subsequent oxidation to the ferric state. Nitric acid is an effective oxidising agent and very convenient to use in this case, owing to the volatility of its decomposition products (oxides of nitrogen), no foreign substances remaining in the final product. Two molecules of nitric acid, in the presence of a reducing agent, decompose thus :

$$2HNO_3 \longrightarrow H_2O + N_2O_5,$$
$$N_2O_5 \longrightarrow 2NO + 3\hat{O}.$$

Each atom of oxygen is able to oxidise 2 molecules of ferrous chloride, according to the equation :

$$2FeCl_2 + 2HCl + \hat{O} = 2FeCl_3 + H_2O,$$

and 3 atoms of oxygen will in this way oxidise 6 molecules of ferrous chloride, so that the whole may be combined into the one equation :

$$6FeCl_2 + 6HCl + 2HNO_3 = 6FeCl_3 + 4H_2O + 2NO.$$

Properties.—A strongly acid, orange-brown solution, with a very astringent taste. Miscible with water and alcohol (90 per cent) in all proportions. The Pharmacopœia gives the specific gravity as about 1·49, but a more usual figure is about 1·45.

Tests for Impurities. *Copper.*—Add excess of ammonium hydroxide and filter. The filtrate should have no blue tinge, and after acidifying with acetic acid should give no brown coloration with potassium ferrocyanide.

Lead.—There should be no turbidity on adding alcohol and dilute sulphuric acid.

Ferrous Salts.—The diluted solution should give no blue precipitate on the addition of potassium ferricyanide.

Add nitric acid and boil, then add ammonium chloride and excess of ammonium hydroxide. Filter, and test the filtrate for the remaining metallic impurities.

Zinc.—Add ammonium sulphide, when there should be no precipitate.

Calcium.—The addition of ammonium oxalate should produce no precipitate.

Sodium and Potassium.—Evaporate a little of the solution to dryness and apply the flame test to the residue, using an indigo prism if necessary.

Ammonium.—Add to the liquor excess of sodium hydroxide, and boil. Test the evolved vapours with turmeric paper (p. 32).

Nitrate (Limit of).—To a well-cooled mixture of equal volumes of concentrated sulphuric acid and a 1-10 dilution of the liquor, add a clear crystal of ferrous sulphate. The crystal should not become brown, nor should a brownish-black colour develop around it.

Arsenic Limit.—10 parts per million (p. 176).

Quantitative Estimation.—The iron is estimated by precipitation as hydroxide and ignition to ferric oxide. Measure 5 mils from

a burette, dilute to about 80 mils, and add excess of ammonium hydroxide. Filter off the precipitate, wash free from chloride, and, without preliminary drying, place the filter and contents in a crucible and ignite, gently at first, and finally to bright redness. Allow to cool, weigh, and repeat the ignition until the weight is constant:

$$FeCl_3 + 3NH_4OH = 3NH_4Cl + Fe(OH)_3,$$
$$2Fe(OH)_3 = Fe_2O_3 + 3H_2O,$$
$$Fe_2O_3 \equiv 2Fe,$$
$$160 \text{ grammes} \equiv 2 \times 56 \text{ grammes of Fe.}$$

The Pharmacopœia requires that the ignited precipitate from 5 mils of the liquor should weigh 1·42 gramme, corresponding to 20 per cent *w/v* of iron, Fe.

Liquor Ferri Perchloridi. *Solution of Ferric Chloride.*—This is made by diluting 1 volume of the strong solution to 4 volumes with water.

Tinctura Ferri Perchloridi. *Tincture of Ferric Chloride.*—This is made by mixing 1 volume of the strong solution and 1 volume of alcohol (90 per cent), and then diluting to 4 volumes with water.

LIQUOR FERRI PERSULPHATIS

Solution of Ferric Sulphate

This solution is included in the Pharmacopœia solely as a source from which freshly precipitated ferric hydroxide may be obtained for use in other preparations.

Preparation.—Ferrous sulphate (400 parts) is dissolved by aid of heat in a mixture of sulphuric acid (37·5 parts) and water (500 parts). This solution is then added to a previously warmed mixture of nitric acid (37·5 parts) and water (100 parts). The mixture is concentrated by boiling until there is a sudden evolution of reddish-brown fumes, and the black liquid becomes red. A few drops of the liquid are now tested for ferrous salt with potassium ferricyanide, and if any be present, a little nitric acid is added and the boiling repeated. Finally, the solution is allowed to cool, and diluted, if necessary, to 550 parts.

The reactions may be explained as follows: The ferrous sulphate is dissolved in sulphuric acid solution to provide the necessary sulphate ions for oxidation to the ferric state. The oxidation is brought about by nitric acid in a similar manner to that described under Liquor Ferri Perchloridi:

$$2FeSO_4 + H_2SO_4 + \hat{O} = Fe_2(SO_4)_3 + H_2O,$$

or expressing the reaction by the usual equation:

$$6FeSO_4 + 3H_2SO_4 + 2HNO_3 = 3Fe_2(SO_4)_3 + 4H_2O + 2NO.$$

The nitric oxide is not liberated at once, but is absorbed by the ferric sulphate solution to form an unstable, dark-coloured compound; as the heating is continued, this compound is decomposed, with sudden evolution of the nitric oxide.

Properties.—An inodorous, dark red solution with an acid reaction. Miscible in all proportions with water and with alcohol (90 per cent). Specific gravity, about 1·441.

Tests for Impurities. *Ferrous Salts.*—Test as under Liquor Ferri Perchloridi Fortis.

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—The iron is estimated as described under Liquor Ferri Perchloridi Fortis, employing the same quantity:

$$Fe_2(SO_4)_3 + 6NH_4OH = 2Fe(OH)_3 + 3(NH)_4SO_4,$$
$$2Fe(OH)_3 = Fe_2O_3 + 3H_2O,$$
$$Fe_2O_3 \equiv 2Fe,$$
$$160 \text{ grammes} \equiv 2 \times 56 \text{ grammes of Fe.}$$

The Pharmacopœia requires that the ignited precipitate obtained from 5 mils of the liquor shall weigh 1·04 grammes.

SYRUPUS FERRI IODIDI

Syrup of Ferrous Iodide

Preparation.—Iron wire (15 parts) and iodine (41·4 parts) are added to 50 parts of water contained in a small, wide-mouthed, loosely corked flask, the mixture being shaken at intervals and very gently warmed, or cooled, as may be necessary. At first a trace of the iodine dissolves in the water, and this reacts with some of the iron to form ferrous iodide (in a solution of which iodine is readily soluble); whereupon considerably more iodine dissolves and a proportionately large portion of the iron is attacked with formation of more ferrous iodide and generation of heat:

$$Fe + I_2 = FeI_2.$$

When the reaction is complete (as shown by the change of colour from brown to a dirty green), glucose (100 parts) is added, the liquid heated on a water-bath for five minutes with frequent shaking, and then filtered into a flask containing about 500 parts of syrup. The flask is rinsed with 25 parts of boiling water, which is poured over the filter and added to the main filtrate, the weight of the whole being then adjusted to 1000 parts with more syrup.

The glucose is included in the preparation on account of its being a powerful reducing agent, thus serving to retard the oxidation which the ferrous iodide is liable to undergo on keeping for any length of time. This oxidation results in the formation of ferric oxyiodide and free iodine, the preparation gradually assuming a brown colour:

$$2FeI_2 + O_2 = 2FeOI + I_2.$$

This change takes place fairly rapidly, even in the presence of glucose, and the syrup should only be stored in such quantities as are likely to be used quickly.

The filtration of the liquid to which the glucose has been added is very slow, and when time is an important factor it is not an uncommon practice for only half the glucose to be dissolved in the liquid to be filtered, the remainder being dissolved in the syrup in which the filtrate is received. This course seems to be open to no particular objection.

Quantitative Estimation.—The ferrous iodide is estimated by precipitation with excess of standard silver nitrate solution and back-titrating with standard ammonium thiocyanate solution. Weigh about 20 grammes of the syrup and dilute to 100 mils. To portions of 20 mils add nitric acid and 20 mils of N/10 silver nitrate solution. Determine the volume of silver nitrate used by adding a few drops of ferric sulphate solution (as indicator) and titrating with N/10 ammonium thiocyanate until a permanent red coloration is obtained. By subtracting the number of mils of thiocyanate required from the volume of silver nitrate solution added, the number of mils of silver nitrate solution required by the ferrous iodide is found:

$$AgNO_3 + NH_4SCN = AgSCN + NH_4NO_3,$$
$$2AgNO_3 + FeI_2 = 2AgI + Fe(NO_3)_2,$$
$$2AgNO_3 \equiv FeI_2,$$
$$2 \times 170 \equiv 310,$$
$$1000 \text{ mils N/1 } AgNO_3 \equiv 155 \text{ grammes of } FeI_2,$$
$$1 \text{ mil N/10 } AgNO_3 \equiv 0{\cdot}0155 \text{ gramme of } FeI_2.$$

Syrupus Ferri Phosphatis. *Syrup of Ferrous Phosphate.*—This is made by adding iron wire (8·6 parts) to 62·5 parts of concentrated phosphoric acid, diluted with an equal volume of water, and contained in a small flask. The mixture is gently heated until all the iron has dissolved, care being taken to avoid undue concentration, and the resulting solution of ferrous phosphate filtered into 700 parts of syrup, the flask and filter being washed with sufficient water to produce 1000 parts of final product:

$$3Fe + 2H_3PO_4 = Fe_3(PO_4)_2 + 3H_2.$$

On keeping, the syrup becomes brown in colour, owing to oxidation of the ferrous salt to the ferric state.

It contains 1·8 per cent of anhydrous ferrous phosphate.

Syrupus Ferri Phosphatis cum Quinina et Strychnina. *Syrup of Phosphate of Iron with Quinine and Strychnine. Unofficial Syns.* Easton's Syrup; Syrupus Tri-phosphatis.—A solution of ferrous phosphate is prepared, in the same manner, and of the same strength, as Syrupus Ferri Phosphatis, but in this case the unfiltered contents of the flask are added to 0·57 parts of strychnine and 14·80 parts of quinine sulphate, which have been triturated

previously with 30 parts of water. These substances dissolve readily in the acid liquid, the strychnine forming strychnine phosphate. When solution is complete, the liquid is filtered into 700 parts of syrup, sufficient water being passed through the filter to produce 1000 parts.

This syrup has a blue fluorescence when freshly prepared, but on keeping becomes brown in colour, owing to the oxidation of the ferrous phosphate.

It is somewhat different from the original formula of Easton, in which the ferrous phosphate was precipitated from ferrous sulphate solution by means of sodium phosphate.

The syrup contains 1·8 per cent *w/v* of anhydrous ferrous phosphate, 1·48 per cent *w/v* of quinine sulphate, and 0·057 per cent *w/v* of strychnine alkaloid.

FERRI PHOSPHAS SACCHARATUS

Saccharated Iron Phosphate

This consists of ferrous phosphate, ferric phosphate, and some iron oxide, mixed with glucose. It is required to contain not less than 60 per cent of ferrous salts calculated as $Fe_3(PO_4)_2,8H_2O$.

Preparation.—Ferrous sulphate (120 parts) is dissolved in a solution of 20 parts of glucose in 400 parts of water. This solution is added to another solution containing 110 parts of sodium phosphate in 400 parts of water, continuous stirring being maintained. To the mixed liquids a solution of 50 parts of sodium carbonate in 400 parts of water is added, and the precipitated ferrous phosphate allowed to subside.

When the ferrous sulphate solution is added to the sodium phosphate solution, free sulphuric acid is formed, and this prevents the complete precipitation of the ferrous phosphate:

$$3FeSO_4 + 2Na_2HPO_4 = Fe_3(PO_4)_2 + 2Na_2SO_4 + H_2SO_4.$$

This difficulty is overcome by making the solution alkaline with sodium carbonate, the sulphuric acid being neutralised.

The precipitate is washed free from most of the sulphate by decantation with two successive quantities of water (washing on a filter is not permissible owing to the ease with which the salt becomes oxidised in air). The precipitate is finally mixed with 20 parts of glucose in order to retard oxidation as far as possible, and dried in a water-oven. When dry it is powdered and preserved in a glass-stoppered bottle.

Properties.—A slate-blue, amorphous powder with a sweetish, chalybeate taste. Partially soluble in water, completely soluble in dilute hydrochloric acid. The hydrochloric acid solution gives deep blue precipitates with both potassium ferrocyanide and potassium ferricyanide, showing the presence of ferric and ferrous iron. When tartaric acid is added to the hydrochloric acid solution, followed by

excess of ammonium hydroxide, then magnesium ammonio-sulphate solution, a white precipitate of magnesium ammonium phosphate, is obtained. The tartaric acid prevents the precipitation of the iron as hydroxide or phosphate.

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—It is not permissible to estimate the iron present by oxidation with acidified potassium permanganate owing to the presence of the glucose, which would reduce this reagent. The iron is therefore estimated by oxidation to the ferric state with potassium dichromate in presence of phosphoric acid. The end point is determined by withdrawing drops of the liquid from time to time on a clean glass rod, and adding to drops of potassium ferricyanide exposed on a white tile. The liquid ceases to yield a blue precipitate with the ferricyanide when all the ferrous salts have been oxidised. When carrying out this estimation it is advisable to perform a rough preliminary titration in order that it shall not be necessary to withdraw an undue quantity of liquid. Weigh about 3 grammes, dissolve in excess of warm concentrated phosphoric acid, allow to cool, and dilute to 100 mils with water. Titrate portions of 20 mils with N/10 potassium dichromate :

$$2Fe_3(PO_4)_2 + K_2Cr_2O_7 + 5H_3PO_4 = 6FePO_4 + 2CrPO_4 + K_2HPO_4 + 7H_2O,$$

$$K_2Cr_2O_7 \equiv 2Fe_3(PO_4)_2,8H_2O$$

$$294 \equiv 2 \times 502,$$

$$1000 \text{ mils N/1 } K_2Cr_2O_7 \equiv \frac{2 \times 502}{6} = 167 \text{ grammes of } Fe_3(PO_4)_2,8H_2O,$$

$$1 \text{ mil of N/10 } K_2Cr_2O_7 \equiv 0{\cdot}0167 \text{ gramme of } Fe_3(PO_4)_2,8H_2O.$$

FERRI CARBONAS SACCHARATUS

Saccharated Iron Carbonate

This consists of more or less oxidised ferrous carbonate mixed with glucose. It is required to contain not less than 50 per cent of ferrous salts calculated as ferrous carbonate, $FeCO_3$.

Preparation.—Ferrous sulphate (97·5 parts) is dissolved in a solution of 15 parts of glucose in 300 parts of water. This solution is added to another solution containing 105 parts of sodium carbonate in 150 parts of water, stirring constantly. Water (400 parts) is then added, and the precipitate of ferrous carbonate allowed to subside:

$$FeSO_4 + Na_2CO_3 = FeCO_3 + Na_2SO_4.$$

The supernatant liquid is decanted and the precipitate washed by decantation with two further quantities, each of 400 parts, of water (washing on a filter is not permissible owing to the ease with which the salt becomes oxidised in air). The precipitate is next

mixed with 15 parts of glucose, dried in a water-oven, powdered, and transferred to a glass-stoppered bottle.

Properties.—A greenish-brown powder with a feebly chalybeate taste. Soluble with effervescence in hydrochloric acid diluted with half its volume of water.

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—It is estimated by oxidation with standard potassium dichromate in precisely the same manner as described for Ferri Phosphas Saccharatus, using the same indicator, and employing the same quantity of substance:

$$3FeCO_3 + 2H_3PO_4 = Fe_3(PO_4)_2 + 3H_2O + 3CO_2,$$

$$2Fe_3(PO_4)_2 + K_2Cr_2O_7 + 5H_3PO_4 = 6FePO_4 + K_2HPO_4 + 2CrPO_4 + 7H_2O,$$

$$K_2Cr_2O_7 \equiv 6FeCO_3,$$

$$294 \equiv 6 \times 116,$$

$$1000 \text{ mils } N/1\ K_2Cr_2O_7 \equiv 116 \text{ grammes of } FeCO_3,$$

$$1 \text{ mil } N/10\ K_2Cr_2O_7 \equiv 0{\cdot}0116 \text{ gramme of } FeCO_3.$$

Scale Preparations of Iron

The three compounds about to be described are the official representatives of a class of compounds comprising iron salts of organic acids, together with other substances, produced in the form of flat, glistening, angular flakes or "scales". The scales are prepared by evaporating a solution of the substance or substances to a syrup and painting this on glass plates. The film is allowed to dry in a dust-free atmosphere and then scraped off. The scales must not be regarded as crystals, for they have no definite structure or definite geometrical shape.

The extensive employment of scale compounds of iron in medicine is based upon their lack of astringency compared with ordinary compounds of iron, and the fact that they may be dispensed with alkaline carbonates or ammonium hydroxide without precipitation of the iron, since the precipitation of ferric hydroxide by ammonium hydroxide is inhibited by the presence in the solution of certain organic compounds containing —OH groups, such as tartaric acid and citric acid; but, of course, when an alkali is added to a solution of a scale compound which contains an alkaloidal salt in addition to the iron compound—Ferri et Quininæ Citras, for example—the free alkaloid is precipitated even though the iron is not.

FERRI ET AMMONII CITRAS

Iron and Ammonium Citrate

Preparation.—The first step is the preparation of freshly precipitated ferric hydroxide by adding 200 parts of Solution of Ferric Sulphate, diluted with 800 parts of water, to 320 parts of Solution

of Ammonia diluted with 800 parts of water, brisk stirring being maintained during the mixing of the liquids. Care must be taken to leave the liquids alkaline as indicated by the odour of ammonia, and to mix the liquids in the order described, for, if the ammonia solution be added to the ferric sulphate solution, some basic sulphate is precipitated, which, being sparingly soluble in citric acid, prevents the formation of transparent scales :

$$Fe_2(SO_4)_3 + 6NH_4OH = 2Fe(OH)_3 + 3(NH_4)_2SO_4.$$

The precipitate is washed free from sulphate by stirring with a large volume of water, allowing to settle, and siphoning off the supernatant liquid, this process being repeated several times. The washed precipitate is collected on a calico filter, squeezed to remove most of the water, and added to a solution of 80 parts of citric acid in an equal quantity of water, kept warm on a water-bath. The mixture is stirred until nearly the whole of the hydroxide has dissolved. If all of it dissolves, more is prepared in the manner described above, and this added also, the object being to ensure the presence of more than sufficient ferric hydroxide to combine with the whole of the citric acid. The solution is cooled, 110 parts of Solution of Ammonia added, and the liquid filtered through flannel. On the large scale, the ferric hydroxide is washed in a filter press.

$$Fe(OH)_3 + H_3C_6H_5O_7 = FeC_6H_5O_7 + 3H_2O,$$
$$FeC_6H_5O_7 + 3NH_4OH = Fe(OH)_3 + (NH_4)_3C_6H_5O_7.$$

The ferric hydroxide shown in the last equation does not appear in the form of a precipitate, but is retained in solution by the ammonium citrate, possibly owing to the formation of a double salt, ferric ammonio-citrate. The filtered liquid is evaporated to a syrupy consistence, the presence of a slight excess of ammonia being maintained, the syrup painted on glass plates and dried in a dust-free atmosphere at a temperature not exceeding 40°, the dried film being afterwards scraped off as flakes.

Properties.—Thin, dark red, transparent scales, with a slightly sweet and astringent taste. Very hygroscopic. Soluble 1-0·5 in water, almost insoluble in alcohol (90 per cent). The aqueous solution is slightly acid.

Tests for Impurities. *Fixed Alkali.*—When ignited it should leave an ash, which, on moistening with water, is not alkaline to litmus. This test is designed to detect the use of sodium or potassium hydroxides instead of ammonium hydroxide as precipitants of the ferric hydroxide. It is very difficult to wash the precipitate free from these impurities, and consequently they appear in the final product as sodium or potassium citrates, which on ignition yield the corresponding carbonates.

Sulphate.—The addition of dilute hydrochloric acid, followed by barium chloride, to a dilute aqueous solution should produce not more than a slight turbidity.

Tartrate.—A 1-10 solution, heated with a slight excess of

potassium hydroxide, evolves ammonia and yields a precipitate of ferric hydroxide. On filtering, the filtrate, acidified with acetic acid, should yield no crystalline precipitate of potassium hydrogen tartrate. This test serves to distinguish Ferri et Ammonii Citras from Ferri et Potassii Tartras, in addition to detecting any substitution of the cheaper tartaric acid for some or all of the citric acid.

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Test.—When incinerated in air, it is required to leave between 31 and 32 per cent of ash, this consisting of ferric oxide, Fe_2O_3.

FERRI ET QUININÆ CITRAS

Iron and Quinine Citrate

Preparation.—A solution of 40 parts of quinine sulphate is prepared by mixing the salt with 320 parts of water and adding 60 parts of dilute sulphuric acid. Slight excess of Solution of Ammonia is added to this, the precipitate of quinine alkaloid collected on a filter, and washed free from sulphate with 1200 parts of water. Freshly prepared ferric hydroxide is then precipitated from 180 parts of Solution of Ferric Sulphate, as described under Ferri et Ammonii Citras, and added to a solution of 123 parts of citric acid in an equal quantity of water, kept warm on a water-bath. When the hydroxide has dissolved, the precipitate of quinine is added and the mixture stirred until this also has dissolved. The liquid is allowed to cool, and a mixture of 60 parts of Solution of Ammonia and 80 parts of water added in small quantities at a time, stirring briskly, and allowing the precipitate of quinine which first appears to dissolve before the next addition. The ammonia is added to nearly neutralise the excess of citric acid, so that the final product consists of a solution of ferric hydroxide in ammonium citrate (p. 134), together with quinine citrate. The solution is filtered, evaporated to a syrupy consistence, and the syrup painted on glass plates and dried at a temperature not exceeding 40°, the resulting film being scraped off to form flakes.

Properties.—Thin, somewhat deliquescent scales of a greenish-yellow colour with a bitter chalybeate taste. Soluble 1-0·5 in water, the solution being slightly acid. The aqueous solution yields a blue precipitate with both potassium ferrocyanide and ferricyanide, showing the presence of ferrous and ferric iron. The ferrous iron is present owing to the fact that citric acid is in excess throughout the manufacture of the scales, causing the reduction of some of the ferric iron. It is due to the presence of ferrous salt that this preparation has a greenish-yellow colour, whereas the colour of Iron and Ammonium Citrate, which contains only ferric iron, is brownish-red. The aqueous solution yields a precipitate of ferric hydroxide and quinine with potassium hydroxide, and a precipitate of quinine with ammonium hydroxide.

Tests for Impurities. *Fixed Alkali.*—Test as under Ferri et Ammonii Citras.

Cinchona Alkaloids other than Quinine.—The precipitate obtained on addition of ammonium hydroxide to the aqueous solution should be almost entirely soluble in a little ether; when incinerated it should only leave a slight residue; and when neutralised with dilute sulphuric acid it should yield the characteristic reactions of quinine sulphate (p. 395).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—When 5 grammes are dissolved in 45 mils of water and treated with slight excess of ammonium hydroxide, the white precipitate obtained, on being extracted with several quantities of chloroform, and these mixed and evaporated, should weigh not less than 0·75 gramme when dried at 110°.

Before attempting this assay the student is recommended to read the chapter on Alkaloidal Assays, and to perform the preliminary experiment described on p. 407.

FERRI ET POTASSII TARTRAS

Iron and Potassium Tartrate
Syns. Ferrum Tartaratum; Tartarated Iron

Preparation.—Ferric hydroxide is freshly precipitated from 200 parts of Solution of Ferric Sulphate, as described under Ferri et Ammonii Citras. The precipitate is intimately mixed with 66·5 parts of potassium hydrogen tartrate and the mixture allowed to stand for twenty-four hours. At the end of this time it is heated to 60°, and as much as possible dissolved in 600 parts of water with constant stirring:

$$KHC_4H_4O_6 + Fe(OH)_3 = K(FeO)C_4H_4O_6 + 2H_2O.$$

The formula of the compound, it will be seen, is analogous to that of antimony potassium tartrate (p. 150). The solution of iron and potassium tartrate is filtered, evaporated at a temperature not exceeding 60° to a syrupy consistence, the syrup painted on glass plates and dried at a temperature not exceeding 40°, the resulting film being scraped off to form scales.

Properties.—Thin, transparent, garnet-red scales with a somewhat sweetish and astringent taste. Soluble in water, but only sparingly soluble in alcohol (90 per cent). The aqueous solution, acidified with hydrochloric acid, gives a blue precipitate with potassium ferrocyanide (presence of ferric iron). A 1-10 solution, boiled with a slight excess of potassium hydroxide, gives a reddish-brown precipitate of ferric hydroxide, and the filtered solution, on slightly acidifying with acetic acid, yields as it cools a crystalline precipitate of potassium hydrogen tartrate (distinction from Ferri et Ammonii Citras).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—When the compound is ignited it leaves a residue of ferric oxide and potassium carbonate. After washing away the carbonate with water and again igniting, with free access of air, a residue of not less than 30 per cent of ferric oxide, Fe_2O_3, should be obtained.

Vinous Preparations of Iron

Two of these are included in the Pharmacopœia, although the first, Vinum Ferri, is now seldom employed in medicine, owing to its variable strength and the time required for its preparation.

VINUM FERRI

Iron Wine

1 part of iron wire is macerated with 20 parts of sherry, when the acetic, malic, and tartaric acids present in the sherry slowly attack some of the iron with formation of soluble salts. The maceration is continued until the filtered liquid responds to the official quantitative test.

In practice, the operation is carried out in a stoppered vessel, from which the stopper is removed occasionally to allow access of air. The iron is kept only partially immersed in the sherry, so as to promote the formation of iron oxide, which is more readily acted upon by the organic acids than is the metal. The process occupies some thirty days.

Quantitative Estimation.—The iron in the wine is estimated gravimetrically as ferric oxide, after decomposing the organic acids by ignition. Measure 50 mils, evaporate to dryness in a dish, and incinerate the residue. Boil the ash with concentrated hydrochloric acid diluted with an equal volume of water, filter, rinse the dish with a little water, and pour through the filter. To the mixed filtrates add a little concentrated nitric acid to oxidise any ferrous salt, boil, add excess of ammonium hydroxide, and collect the precipitated ferric hydroxide on a filter. Wash the precipitate with water until free from chloride, and, without separating from the filter-paper, ignite in a crucible, cool, and weigh, repeating the ignition until the weight is constant:

$$2Fe(OH)_3 = Fe_2O_3 + 3H_2O,$$
$$Fe_2O_3 \equiv 2Fe,$$
$$160 \text{ grammes} \equiv 112 \text{ grammes of Fe.}$$

The Pharmacopœia requires that the residue obtained in this way from 50 mils of the wine shall weigh between 0·089 and 0·215 gramme, corresponding to 0·125-0·300 per cent *w/v* of Fe.

Vinum Ferri Citratis. *Wine of Iron Citrate.*—This is prepared by dissolving 18 parts of iron and ammonium citrate in sufficient

orange wine to produce 1000 parts. The solution is shaken occasionally during three days and filtered.

COMPOUNDS OF ALUMINIUM

Al (Atomic Wt. = 27)

The element aluminium, in the form of its silicates, is the chief constituent of the *clays* and *felspars* which form so large a proportion of the earth's crust. The mineral *kaolin*, which has already been described (p. 49), consists almost entirely of hydrated aluminium silicate. Unfortunately, practical difficulties prohibit the economical extraction of this very useful metal from these sources, and, commercially, it is almost exclusively obtained from the mineral *bauxite*, $Al_2O_3,2H_2O$, by an electrolytic process.

General Tests for Aluminium.—(1) An aluminium compound, heated on a charcoal block in a blowpipe flame, then moistened with cobalt nitrate solution and again heated, gives a blue mass (Thenard's blue). But a somewhat similar colour is given by certain borates, silicates, phosphates, and arsenates.

(2) A solution of an aluminium salt yields with ammonium hydroxide a flocculent precipitate of aluminium hydroxide, $Al(OH)_3$. Sodium hydroxide also produces a precipitate of aluminium hydroxide, but this is readily soluble in excess of the reagent owing to the formation of sodium aluminate, $Al(ONa)_3$. The hydroxide is reprecipitated on adding ammonium chloride and boiling:

$$Al(ONa)_3 + 3NH_4Cl = Al(OH)_3 + 3NaCl + 3NH_3.$$

ALUMEN PURIFICATUM

Purified Alum

The Pharmacopœia permits the use of either

Potassium alum, $K_2SO_4,Al_2(SO_4)_3,24H_2O$, or
Ammonium alum, $(NH_4)_2SO_4,Al_2(SO_4)_3,24H_2O$,

under the name of purified alum.

Preparation.—When a solution of potassium sulphate is mixed with a solution of aluminium sulphate, in molecular proportions, the liquids concentrated and allowed to crystallise, the product is a "double salt", consisting of 1 molecule of each salt crystallised together with 24 molecules of water, and belongs to the class of compounds called the alums. When potassium sulphate is employed, the product is "potassium alum", and when ammonium sulphate is used, "ammonium alum". On the large scale the solutions of the proper strength are mixed and concentrated to a specific gravity which has been found by experience to give the best yield;

the liquid is then transferred to a barrel to crystallise. After a time the staves are broken off, exposing a barrel-shaped mass of alum crystals. A hole is bored through this, the mother liquor in the centre run off to be further concentrated, and the mass is then broken up to form the familiar crystals of commerce.

Properties.—Large, colourless, transparent, octahedral crystals, or crystalline masses, with a sweet, very astringent taste. Soluble 1·10 in water, the solubility increasing rapidly with rise of temperature. The aqueous solution has an acid reaction owing to partial hydrolysis. The surface of alum crystals may sometimes be slightly efflorescent, due to the formation of basic salt, and this should be removed by washing, and the crystals dried on filter-paper before being used for official purposes. Commercial powdered alum often contains considerable quantities of this impurity, and will not form a clear solution with water; it should not be employed for medicinal purposes. On heating, alum loses its water of crystallisation, and on strongly heating partially decomposes, with formation of some sulphuric acid and a basic sulphate.

Tests for Impurities. (To be applied to the aqueous solution.) *Copper.*—Add a few drops of nitric acid and boil, then add ammonium hydroxide in excess, and filter. The filtrate should have no blue tinge and, on acidifying with acetic acid and adding potassium ferrocyanide, should not acquire a brown colour.

Lead.—Add ammonium hydroxide and potassium cyanide, then a drop of sodium sulphide, when there should be no dark coloration.

Iron.—Add nitric acid, boil, and add potassium ferrocyanide, when there should not be more than the slightest blue or green colour.

Boil the solution with a few drops of nitric acid, and add ammonium chloride and excess of ammonium hydroxide. Filter off the precipitated aluminium hydroxide and test the filtrate for the following metallic impurities:

Zinc.—The addition of ammonium sulphide should produce no precipitate.

Calcium.—Add ammonium oxalate, when there should be no precipitate.

Sodium.—Apply the flame test to the dry salt.

Arsenic Limit.—5 parts per million (p. 176).

Alumen Exsiccatum. *Exsiccated Alum.*—This consists of potassium alum which has been deprived of its water of crystallisation by means of heat. Ammonium alum cannot be employed, as it decomposes on heating.

Preparation.—A weighed quantity of potassium alum is heated in a porcelain dish until it liquefies, when it is heated more strongly, until water-vapour ceases to be evolved and the salt has lost from 45 to 46 per cent of its weight. Care must be taken that the temperature does not rise above 200° during the process, or the

salt may be partially decomposed with formation of sulphuric acid and some insoluble basic sulphate.

Properties.—A white, amorphous powder, slowly but completely soluble 1-20 in water.

Tests for Impurities.—It should be free from the impurities mentioned under Alumen Purificatum, and should be completely soluble in water, showing the absence of insoluble basic sulphate.

Glycerinum Aluminis. *Glycerin of Alum.*—20 parts of alum are dissolved in a mixture of 7·5 parts of water and 120 parts by volume of glycerin by aid of very gentle heat, if necessary. The solution is set aside and the clear liquid poured off from any deposit of basic salt. It is advisable to select clean crystals of ammonium alum, wash in a little cold water, dry on a filter-paper, powder, and weigh, solution being effected in a warm mortar.

COMPOUNDS OF CHROMIUM

Cr (Atomic Wt. = 52)

The chief natural source of chromium is *chrome iron ore*, FeO,Cr_2O_3, which is a heavy, black, insoluble mineral, and from this chromium is extracted in the form of chromate by roasting with alkalies in the presence of air.

Only two compounds of chromium are official, and one of these, Potassii Bichromas, has already been dealt with (p. 63).

General Tests for Chromium.—(1) A chromium salt, on fusion with sodium carbonate and a little potassium chlorate or nitrate (as oxidising agent), yields a yellow mass of sodium chromate.

(2) A solution of a chromium salt gives, on addition of excess of ammonium hydroxide, a bluish-green precipitate of chromium hydroxide, slightly soluble in excess of the reagent with formation of a violet solution. The precipitate is not appreciably soluble in sodium hydroxide (distinction from aluminium), but when suspended in water, treated with excess of sodium peroxide, and boiled, it dissolves to form a yellow solution of sodium chromate (distinction from iron).

(3) In the case of chromates or dichromates the chromium is part of the acidic radicle Aqueous solutions of these salts are yellow or orange in colour respectively; they give with barium chloride a yellow precipitate of barium chromate, insoluble in acetic acid, but readily soluble in dilute hydrochloric acid.

Chromates and dichromates can be reduced by boiling for some time with concentrated hydrochloric acid, or by passing sulphur dioxide or hydrogen sulphide through the aqueous solution. After reduction, the solution is green and gives the reactions of chromium salts :

$$K_2Cr_2O_7 + 14HCl = 2KCl + 2CrCl_3 + 3Cl_2 + 7H_2O.$$

ACIDUM CHROMICUM

Chromic Anhydride, CrO_3. (Mol. Wt. = 100.) *Syn.* Chromic Acid

Preparation.—To a solution of 15 parts of potassium dichromate in 25 parts of water, 21 parts of concentrated sulphuric acid is added, and the mixture allowed to stand for twelve hours :

$$K_2Cr_2O_7 + 2H_2SO_4 = 2CrO_3 + 2KHSO_4 + H_2O.$$

The liquid is filtered from the crystals of potassium hydrogen sulphate, heated on a water-bath, and treated with 7·5 parts of sulphuric acid, followed by enough water to dissolve the precipitated chromic anhydride. On cooling and allowing to stand, the chromic anhydride crystallises out and is filtered off ; a further quantity may be obtained by concentration of the mother liquor. After draining well, the crystals are washed with a little concentrated nitric acid, dried in a current of warm air, and transferred immediately to a well-stoppered bottle. Ordinary filter-paper must not be employed in these operations since the chromic anhydride is reduced by organic matter. Glass wool or asbestos is usually employed.

Properties.—Crimson, needle-shaped, very deliquescent crystals. Very soluble in water and in ether. On heating it melts at about 192°, and at a higher temperature decomposes with evolution of oxygen, leaving a green residue of chromic oxide :

$$4CrO_3 = 2Cr_2O_3 + 3O_2.$$

Chromic anhydride is a very powerful oxidising agent. When warmed with hydrochloric acid, chlorine is evolved, and if brought into contact with small quantities of alcohol, ether, or glycerin, oxidation proceeds so rapidly that sudden combustion or explosion may result. It has a highly corrosive action on vegetable and animal tissues. Chromic anhydride should be kept in a well-stoppered bottle.

Test for Impurity. *Sulphate* (*Limit of*).—Dissolve 4 grammes in a mixture of 20 mils of water and 10 mils of concentrated hydrochloric acid. Add 5 mils of 10 per cent barium chloride solution, and filter. The filtrate should yield no further precipitate on the addition of more barium chloride.

Liquor Acidi Chromici. *Solution of Chromic Acid.*—This is a simple 25 per cent *w/v* solution of chromic anhydride. It has a yellow colour and contains free chromic acid :

$$CrO_3 + H_2O = H_2CrO_4.$$

ACIDUM ARSENIOSUM

Arsenious Anhydride, As_4O_6. (Mol. Wt. = 396)

Syns. Arsenic ; Arsenious Acid

Unofficial Syns. White Arsenic ; Arsenious Oxide

This is required to contain not less than 99·8 per cent of arsenious oxide, As_4O_6.

Preparation.—It is manufactured by roasting arsenical ores, the most commonly employed being mispickel and leucopyrite. If leucopyrite be used the reaction may be represented thus :

$$4FeAs_2 + 9O_2 = 2Fe_2O_3 + 2As_4O_6.$$

When mispickel is employed, arsenious oxide and sulphur dioxide are given off at a red heat, leaving a residue of iron oxide, sulphate, and arsenate.

The roasting is frequently carried out in a reverberatory furnace, though a purer product is obtained if a muffle furnace be used. The arsenious oxide is collected as a sublimate in specially designed chambers and flues, and is purified by sublimation from iron vessels.

Properties.—Arsenious oxide occurs in two forms—one a white, opaque, crystalline powder, and the other a transparent, vitreous, and often stratified variety. The official substance often contains both varieties. Very slowly soluble about 1-65 in water, the solubility varying according to the proportion of each variety present, the vitreous form being more soluble in cold water than the crystalline ; in some samples, the solubility may be nearer 1-100. The aqueous solution is odourless, tasteless, and faintly acid to litmus. When heated in a dry tube, arsenious oxide sublimes, condensing on the cool portions of the tube in the form of small, glistening, transparent, octahedral crystals.

The oxide is amphoteric, but most of its properties are those of an acidic oxide. It dissolves freely in solutions of sodium, potassium, and ammonium hydroxides, and of alkali carbonates, with formation of the corresponding arsenites :

$$12NaOH + As_4O_6 = \underset{\text{Sodium arsenite.}}{4Na_3AsO_3} + 6H_2O.$$

Its very feeble basic character is shown by the fact that, although it dissolves freely in concentrated hydrochloric acid with formation of arsenious chloride, on diluting the solution and boiling, this undergoes hydrolysis :

$$As_4O_6 + 12HCl \rightleftharpoons 4AsCl_3 + 6H_2O.$$

Tests for Impurities. *Non-volatile Matter.*—When heated in a dry tube it should volatilise completely.

Arsenious Sulphide.—It should dissolve completely in ammonium hydroxide, and when the solution is diluted with an

equal volume of water and acidified with hydrochloric acid, there should be no yellow colour.

Quantitative Estimation.—Arsenious oxide is estimated by dissolving in sodium hydroxide to form sodium arsenite, and oxidising this to the arsenate by means of standard iodine:

$$\text{(i.)}\quad As_4O_6 + 12NaOH = 4Na_3AsO_3 + 6H_2O,$$
$$\text{(ii.)}\quad Na_3AsO_3 + H_2O + I_2 \rightleftharpoons Na_3AsO_4 + 2HI.$$

In carrying out this estimation it is essential that no free sodium hydroxide shall be left in the solution, as this would react with some of the iodine:

$$6NaOH + 3I_2 = NaIO_3 + 5NaI + 3H_2O.$$

On the other hand, the hydriodic acid produced during the oxidation must be neutralised as soon as formed, because the reaction represented in equation (ii.) is a reversible one. These difficulties are overcome by first neutralising the excess of sodium hydroxide with hydrochloric acid, and then adding sodium bicarbonate before titrating.

Weigh about 0·5 gramme of the oxide, dissolve in boiling water containing a little sodium hydroxide, cool, make just acid with hydrochloric acid, add excess of a cold, freshly prepared solution of sodium bicarbonate, and dilute to 100 mils. Titrate portions of 20 mils with N/10 iodine until the iodine is no longer decolorised.

From equations (i.) and (ii.):

$$4I_2 \equiv As_4O_6,$$
$$8 \times 127 \equiv 396,$$
$$1000 \text{ mils } N/1\ I_2 \equiv \frac{396}{8} = 49{\cdot}5 \text{ grammes of } As_4O_6,$$
$$1 \text{ mil } N/10\ I_2 \equiv 0{\cdot}00495 \text{ gramme of } As_4O_6.$$

Liquor Arsenicalis. *Arsenical Solution.* *Syn.* Fowler's Solution.—This is a 1 per cent *w/v* solution of arsenious oxide prepared by dissolving 1 part of arsenious anhydride and 1 part of potassium carbonate in 50 parts of water by aid of heat. Solution is effected more quickly if the two solids be previously intimately mixed in a mortar, and if the liquid be brought to the boiling-point and then allowed to simmer; violent ebullition is not only unnecessary, but concentrates the liquid unduly. When the arsenious anhydride has dissolved, the solution is cooled and filtered, before the addition of 3 parts of compound tincture of lavender, and adjustment to 100 parts with water.

The potassium carbonate facilitates the solution of the arsenious anhydride, presumably owing to the formation of potassium arsenite:

$$6H_2O + As_4O_6 = 4H_3AsO_3,$$
$$2H_3AsO_3 + 3K_2CO_3 = 2K_3AsO_3 + 3CO_2 + 3H_2O.$$

Properties.—A reddish liquid, alkaline to litmus, and having the

odour of lavender. On keeping, a flocculence may develop, due to the action of the weak alkaline solution on the glass of the container. In dispensing, the solution must be neutralised with a little dilute hydrochloric acid if prescribed with alkaloidal salts, for otherwise the free alkaloid will be liberated, and, if there is not sufficient water present to keep it in solution, will be precipitated.

Quantitative Estimation.—The solution is estimated in the manner described under Acidum Arseniosum, employing 20 mils for each titration, the liquid being previously neutralised with hydrochloric acid, and a slight excess of sodium bicarbonate being maintained whilst titrating with the N/10 iodine.

Liquor Arsenici Hydrochloricus. *Hydrochloric Solution of Arsenic.*—This is a 1 per cent *w/v* solution of arsenious oxide prepared by dissolving 1 part of arsenious anhydride and 1·2 parts of hydrochloric acid in 50 parts of water by aid of heat, cooling, filtering, and adjusting the volume to 100 parts with water. The hydrochloric acid assists the solution of the arsenic, presumably owing to the formation of arsenious chloride, which, however, undergoes hydrolysis :

$$As_4O_6 + 12HCl \rightleftharpoons 4AsCl_3 + 6H_2O.$$

Properties.—The liquid is colourless and acid to litmus. It is intended to be prescribed when arsenic is required in conjunction with alkaloidal salts or acid substances, with which Liquor Arsenicalis would be incompatible.

Quantitative Estimation.—As for Liquor Arsenicalis.

ARSENII IODIDUM

Arsenious Iodide, AsI_3. (Mol. Wt. = 456)

Preparation.—(1) Powdered arsenic—the element (1 part)—and iodine (5 parts) are thoroughly mixed in a mortar, and the mixture very gently heated in a small flask until quite molten, when it is poured out on to a porcelain tile and allowed to solidify. The product is purified by finely powdering, extracting with chloroform, filtering, and evaporating the solvent, when the arsenious iodide is obtained as a crystalline powder, which is washed with a little more chloroform and dried :

$$2As + 3I_2 = 2AsI_3.$$

Carbon disulphide, toluene, or certain other solvents may be used in place of chloroform.

(2) It can also be prepared by adding a solution of 1 part of arsenious oxide in 25 parts of hydrochloric acid to a hot solution of 5 parts of potassium iodide in 4 parts of water. The liquid is allowed to cool, shaken with chloroform, and the arsenious iodide obtained from the chloroform solution by crystallisation :

$$As_4O_6 + 12HCl + 12KI = 4AsI_3 + 12KCl + 6H_2O.$$

Properties.—The official substance occurs in small orange-coloured crystals; but commercial samples frequently consist of crystalline masses which have not been purified by crystallisation and consequently contain free iodine and arsenic. Soluble in water and in alcohol (90 per cent), the aqueous solution being acid to litmus owing to partial hydrolysis:

$$4AsI_3 + 6H_2O \rightleftharpoons 12HI + As_4O_6.$$

The aqueous solution should be practically colourless. When heated, the salt volatilises completely, with partial decomposition and liberation of iodine.

Liquor Arsenii et Hydrargyri Iodidi. *Solution of Arsenious and Mercuric Iodides.* *Syn.* Donovan's Solution.—This is prepared by triturating 1 part of arsenious iodide and 1 part of mercuric iodide with 25 parts of water until dissolved, then filtering and passing sufficient water through the filter to produce 100 parts of the solution.

It is advisable to allow the mixture of the salts with the first quantity of water to stand for half an hour before filtering. The arsenious iodide undergoes hydrolysis with formation of hydriodic acid:

$$4AsI_3 + 6H_2O = As_4O_6 + 12HI,$$

and the ordinarily insoluble mercuric iodide dissolves in the hydriodic acid solution owing to the formation of a soluble double salt:

$$HgI_2 + 2HI = HgI_2,2HI.$$

The double salt is less toxic than mercuric iodide, and the solution may be given in larger doses than the quantity of mercuric iodide used in its preparation would seem to permit. The residue on the filter-paper is said to be one of elementary arsenic.

COMPOUNDS OF ANTIMONY

Sb (Atomic Wt. = 120)

The chief mineral source of antimony is the trisulphide known as *stibnite* or *antimony glance*, Sb_2S_3, which, unlike the artificially prepared compound, is crystalline and greyish-black in colour. Other antimony minerals are of relatively little importance as a source of the metal, although the oxide, Sb_2O_3, is fairly widely distributed.

Of the oxides of antimony, two, the trioxide, Sb_2O_3, and the pentoxide, Sb_2O_5, resemble the corresponding oxides of arsenic in being amphoteric, although the basic characters of the trioxide are somewhat more strongly marked than those of the corresponding arsenic compound. Either of the oxides, on heating in air, is converted into the tetroxide, Sb_2O_4.

General Tests for Antimony.—(1) Antimony compounds, when mixed with sodium carbonate and potassium cyanide and heated on charcoal in the blowpipe flame, produce globules of the metal, which are brittle, and on breaking have a crystalline appearance. If heating be continued, the metal burns, with production of white fumes of antimonious oxide and the formation of an encrustation on the charcoal.

(2) Hydrogen sulphide, passed through a solution of an antimony compound in dilute hydrochloric acid, produces an orange precipitate of antimony trisulphide. The precipitate is insoluble in oxalic acid solution, but dissolves in concentrated hydrochloric acid with formation of antimony trichloride, and in yellow ammonium sulphide with formation of complex thio-salts of antimony. When the ammonium sulphide solution is acidified, the pentasulphide is precipitated.

(3) The addition of iron wire to a solution of an antimony salt in dilute hydrochloric acid, followed by boiling, results in the separation of a thick, flaky, black precipitate of metallic antimony.

(4) On applying Marsh's Test (p. 142), antimony salts give a similar stain to that of arsenic, but distinguishable by its insolubility in a solution of chlorinated lime.

ANTIMONII OXIDUM

Antimonious Oxide, Sb_2O_3. (Mol. Wt. =288)

Preparation.—A concentrated aqueous solution of antimonious chloride is poured into excess of hot water, when hydrolysis occurs and antimony oxychloride is precipitated:

$$SbCl_3 + H_2O = SbOCl + 2HCl.$$

In order to neutralise the free hydrochloric acid and to effect the complete hydrolysis of the oxychloride, sodium carbonate is added and the mixture is boiled:

$$2SbOCl + Na_2CO_3 = Sb_2O_3 + 2NaCl + CO_2.$$

The precipitate is collected on a filter, washed, and dried.

Properties.—A greyish-white powder, which melts at a dull red heat. Insoluble in water. Soluble in hydrochloric acid with formation of antimony trichloride; and on pouring the acid solution into water a white precipitate of oxychloride is obtained. On heating in air it is converted into the tetroxide, Sb_2O_4.

Tests for Impurities. *Lead and Copper.*—Warm with sodium hydroxide solution to which a few drops of ammonium hydroxide have been added. Filter, and add to the filtrate a few drops of sodium sulphide solution, when there should be no dark coloration.

Arsenic.—Apply Fleitmann's Test (p. 143).

Iron.—Dissolve in dilute nitric acid, and add potassium ferro-

cyanide, when there should not be more than a slight blue or green colour.

Dissolve some of the substance in the minimum quantity of dilute hydrochloric acid, dilute the solution somewhat, and pass hydrogen sulphide until all the antimony has been precipitated. Filter. After boiling off all the hydrogen sulphide, test the filtrate for the following metallic impurities:

Calcium.—Add ammonium chloride, ammonium hydroxide in excess, and ammonium oxalate, when there should be no precipitate.

Sodium and Potassium.—Evaporate to dryness and apply the flame test to the residue, using an indigo prism if necessary.

Sulphate and Chloride.—Dissolve some of the oxide in dilute nitric acid and add to separate portions of the solution barium chloride and silver nitrate, which should produce not more than a slight turbidity or a slight opalescence respectively.

Antimonic Compounds.—The oxide should dissolve completely in acid potassium tartrate solution (forming tartarated antimony).

Quantitative Estimation.—It is estimated by oxidation with standard iodine, the reactions being similar to those which take place in the estimation of Acidum Arseniosum. The method of preparing the solution has to be modified in this case because the neutralisation of a solution of this oxide in sodium hydroxide, or the addition of sodium bicarbonate to an acid solution of the oxide, results in the precipitation of the antimony as a basic salt.

This difficulty is overcome by the addition of sodium potassium tartrate, which prevents the precipitation, owing to the formation of soluble sodium and potassium antimonyl tartrates. Weigh about 1 gramme, dissolve in a little fairly concentrated hydrochloric acid, add a concentrated solution of about 10 grammes of sodium potassium tartrate, then a slight excess of cold solution of sodium bicarbonate, and adjust the volume to 100 mils. Titrate portions of 20 mils with N/10 iodine:

$$Sb_2O_3 + 2H_2O + 2I_2 = Sb_2O_5 + 4HI,$$
$$2I_2 \equiv Sb_2O_3,$$
$$4 \times 127 = 288,$$
$$1000 \text{ mils N/1 } I_2 \equiv \frac{288}{4} = 72 \text{ grammes of } Sb_2O_3,$$
$$1 \text{ mil N/10 } I_2 \equiv 0{\cdot}0072 \text{ gramme of } Sb_2O_3.$$

ANTIMONIUM SULPHURATUM

Sulphurated Antimony

This is a mixture, containing antimony trisulphide and pentasulphide, trioxide and pentoxide, with some free sulphur.

Preparation.—It is obtained by decomposing with acid a solution of antimony thio-salts. As the composition of the product

varies according to the procedure, the pharmacopœial method must be adhered to.

Black antimonious sulphide (2 parts) and sublimed sulphur (2 parts) are mixed with 1 part of commercial caustic soda dissolved in 20 parts of water. The mixture is boiled for two hours with frequent stirring, the water lost by evaporation being replaced from time to time. While still hot, 36 parts of boiling water is added, and the product strained through calico. To the hot, strained liquid a slight excess of dilute sulphuric acid is added gradually, the precipitate collected on a calico filter, washed free from sulphate, and dried in a water-oven.

Kermes mineral, which was once widely employed in medicine, is a preparation obtained by a process similar to that described above, but omitting the sulphur.

Properties.—A tasteless, odourless, orange-red, amorphous powder. Insoluble in water. Readily soluble in sodium hydroxide solution. It is decomposed by hot concentrated hydrochloric acid with evolution of hydrogen sulphide and separation of sulphur.

Tests for Impurities. *Sulphate (Limit of).*—Digest 1 gramme with 20 mils of hot water, filter, acidify the filtrate with dilute nitric acid, and add barium chloride, when the liquid should not become more than slightly cloudy.

Arsenic Limit.—1000 parts per million (p. 176).

Quantitative Test.—The antimony present may be estimated gravimetrically by oxidation to the pentoxide, Sb_2O_5, and conversion of this into the tetroxide by heating. Weigh about 3 grammes, moisten with dilute nitric acid, then warm with successive quantities of fuming nitric acid until red fumes are no longer evolved. Dry, cautiously heat to redness, and weigh:

$$Sb_2O_4 \equiv 2Sb,$$
$$304 \text{ grammes} \equiv 240 \text{ grammes}.$$

The Pharmacopœia requires that 3 grammes, treated in this way, shall yield a residue weighing between 1·6 and 1·8 grammes.

ANTIMONIUM TARTARATUM

Tartarated Antimony $[K(SbO)C_4H_4O_6]_2,H_2O$. (Mol. Wt. = 664.)
Syns. Tartar Emetic; Potassio-tartrate of Antimony

This is required to contain not less than 99 per cent of $[K(SbO)C_4H_4O_6]_2,H_2O$.

Preparation.—Antimony oxide (5 parts) and finely powdered acid potassium tartrate (6 parts) are made into a paste with water and set aside for twenty-four hours; about 40 parts of water is then added, and the mixture boiled for fifteen minutes, with frequent stirring. The hot liquid is filtered, the filtrate set aside to crystallise, and the crystals collected on a filter-paper and dried at ordinary

temperature on a porous plate. On concentration of the mother liquor, a further quantity is obtained.

Properties.—Colourless, transparent crystals having triangular facets. Taste, sweet and metallic. Soluble 1·17 in water, and 1·3 in boiling water, the aqueous solution being slightly acid: almost insoluble in alcohol (90 per cent), but fairly soluble in diluted alcohol. It is precipitated from its solutions by tannic acid. On heating to redness, it chars, leaving a residue of potassium carbonate, oxide of antimony, and carbon.

Tests for Impurities. *Lead, Copper, Arsenic, Iron, and Sodium.*—There should be no indication of these on testing as described under Antimonii Oxidum.

Ammonium.—Boil with sodium hydroxide solution and test the evolved vapours with turmeric paper (p. 32).

Sulphate and Chloride.—There should be no indication of these on testing as under Antimonii Oxidum.

Acid Potassium Tartrate.—The compound should not cause effervescence when shaken with a cold solution of sodium bicarbonate.

Quantitative Estimation.—This compound is estimated by oxidation with standard iodine as described under Antimonii Oxidum. Weigh about 2 grammes, dissolve in water, and dilute to 100 mils. To portions of 20 mils of this solution, add about 3 grammes of sodium potassium tartrate and about 2 grammes of sodium bicarbonate, and then titrate with N/10 iodine:

$$2K(SbO)C_4H_4O_6 + 2I_2 + 3H_2O = 2KHC_4H_4O_6 + Sb_2O_5 + 4HI,$$
$$2I_2 \equiv [K(SbO)C_4H_4O_6]_2,H_2O,$$
$$4 \times 127 \equiv 664,$$
$$1000 \text{ mils } N/1\ I_2 \equiv \frac{664}{4} = 166 \text{ grammes of } [K(SbO)C_4H_4O_6]_2,H_2O,$$
$$1 \text{ mil } N/10\ I_2 \equiv 0{\cdot}0166 \text{ gramme of } [K(SbO)C_4H_4O_6]_2,H_2O.$$

COMPOUNDS OF BISMUTH

Bi (Atomic Wt. = 208)

Bismuth generally occurs in the free state, but it is also found as *bismuth glance*, Bi_2S_3, and *bismuth ochre*, Bi_2O_3.

It forms a stable trioxide, Bi_2O_3, which is more decidedly basic in character than the corresponding antimony compound; other oxides, Bi_2O_2, Bi_2O_4, and Bi_2O_5, are known.

General Tests for Bismuth.—(1) When a bismuth compound is heated with sodium carbonate on charcoal in the blowpipe flame, brittle beads of the metal are produced, together with a yellow encrustation of the trioxide.

(2) Hydrogen sulphide passed through a solution of a bismuth compound in dilute hydrochloric acid, produces a dark brown precipitate of the sulphide, Bi_2S_3, insoluble in yellow ammonium sulphide, but soluble in boiling dilute nitric acid.

(3) Ammonium hydroxide gives, with a solution of a bismuth salt, a white precipitate of the hydroxide, $Bi(OH)_3$. The precipitate is soluble in dilute hydrochloric acid, and this solution, when poured into a large volume of water, gives a white turbidity, due to the formation of the oxychloride:

$$BiCl_3 + H_2O \rightleftharpoons BiOCl + 2HCl.$$

BISMUTHI CARBONAS

Bismuth Oxycarbonate, $(Bi_2O_2CO_3)_2,H_2O$. (Mol. Wt. = 1034.)
Syn. Bismuth Subcarbonate

Preparation.—Metallic bismuth is dissolved in 50 per cent nitric acid, and the solution evaporated to small bulk:

$$2Bi + 8HNO_3 = 2Bi(NO_3)_3 + 2NO + 4H_2O.$$

The solution is then added gradually, with constant stirring, to a cold solution of ammonium carbonate:

$$2Bi(NO_3)_3 + 2NH_4HCO_3,NH_4NH_2CO_2 + H_2O = 6NH_4NO_3 + Bi_2O_2CO_3 + 3CO_2.$$

The precipitated oxycarbonate is collected on a calico filter, well washed with water, and dried at a temperature not exceeding 65°.

Properties.—A white, tasteless powder of varying density. Insoluble in water; soluble in acids, with effervescence. On exposure to air containing hydrogen sulphide it slowly darkens. When heated, it loses carbon dioxide and water, leaving a yellow residue of the trioxide.

Tests for Impurities. *Silver and Lead.*—Dissolve about 2 grammes in the minimum quantity of nitric acid, and pour the solution into about 100 mils of water, in order to precipitate most of the bismuth as oxynitrate. Filter, evaporate the filtrate to about 20 mils, and again filter. Divide the filtrate into two parts.

(i.) Heat to boiling and add hydrochloric acid. There should be no opalescence (absence of silver).

(ii.) Add an equal volume of alcohol and a little dilute sulphuric acid, then allow to stand. There should be no turbidity (absence of lead).

Copper.—Dissolve in hydrochloric acid, add excess of ammonium hydroxide, and filter. The filtrate should have no blue tinge, and should give no brown coloration on acidifying with acetic acid and adding potassium ferrocyanide.

Selenium and Tellurium.—Dissolve in concentrated nitric acid, add ammonium chloride solution, dilute well, and filter. Add to the filtrate excess of sodium sulphite solution and allow to stand. There should be no precipitate or coloration, even after twelve hours (due to reduction to metallic selenium or tellurium).

Calcium.—Boil with dilute hydrochloric acid, dilute well, and,

without filtering, pass hydrogen sulphide. Filter off the precipitate, which will contain the bismuth, together with any of the previously mentioned metallic impurities, and add to the filtrate ammonium hydroxide in excess and ammonium oxalate. There should be no precipitate.

Sulphate.—Dissolve in excess of a mixture of equal volumes of concentrated hydrochloric acid and water, and add barium chloride, when there should be not more than a slight turbidity.

Chloride.—Dissolve in concentrated nitric acid, and add silver nitrate solution, when there should be no opalescence.

Alkaline Carbonates (*Limit of*).—Boil 5 grammes with water and filter. The filtrate should not require more than 1 mil of N/10 sulphuric acid for neutralisation, using methyl orange as indicator.

Nitrate (*Limit of*).—Commercial samples generally contain traces of nitrate. The Pharmacopœia states that, on mixing 0·02 gramme with 5 drops of phenol-disulphonic acid, adding, after five minutes, 10 mils of Solution of Ammonia, filtering, washing the precipitate with water, and adding water to the filtrate until it measures 100 mils, the colour of the filtrate should not be deeper than that obtained by similarly treating 0·00013 gramme of potassium nitrate. This limit is equivalent to 2 per cent of bismuth oxynitrate.

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Test.—When strongly heated it should yield between 89 and 91 per cent of bismuth oxide, Bi_2O_3.

BISMUTHI SUBNITRAS

Bismuth Oxynitrate, $BiONO_3,H_2O$. (Mol. Wt. = 304)

Preparation.—Metallic bismuth is dissolved in 50 per cent nitric acid :

$$2Bi + 8HNO_3 = 2Bi(NO_3)_3 + 2NO + 4H_2O,$$

and the solution evaporated to small bulk, then poured into a large excess of water :

$$Bi(NO_3)_3 + H_2O = BiONO_3 + 2HNO_3.$$

The precipitate is allowed to subside, washed by decantation, collected on a calico filter, and dried at a temperature not exceeding 65°.

Properties.—A white, tasteless, microcrystalline powder, almost insoluble in water, and very slightly acid to litmus, owing to hydrolysis, so that when added to solutions of alkaline carbonates or bicarbonates it causes an evolution of carbon dioxide : in dispensing, the completion of this reaction may be hastened by the use of warm water. On heating, the salt evolves oxides of nitrogen and leaves a residue of bismuth oxide, Bi_2O_3.

Tests for Impurities. *Silver, Lead, Copper, Selenium, Tellurium, Calcium, and Sulphate.*—Test as described under Bismuthi Carbonas.

Chloride.—There should not be more than a slight opalescence when tested as under Bismuthi Carbonas.

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Test.—When strongly heated, it should leave from 79 to 82 per cent of bismuth oxide, Bi_2O_3.

LIQUOR BISMUTHI ET AMMONII CITRATIS

Solution of Bismuth and Ammonium Citrate

Preparation.—Citric acid is mixed in a mortar with bismuth oxynitrate and water, and the mixture set aside, with occasional stirring, for half an hour, or until a little on trial is completely soluble in Solution of Ammonia :

$$H_3C_6H_5O_7 + BiONO_3 = BiC_6H_5O_7 + HNO_3 + H_2O.$$

The bismuth citrate is washed free from nitrate by decantation, and, while still moist, is dissolved in the minimum quantity of Solution of Ammonia and made up to volume with water. The ammonia produces bismuth hydroxide :

$$BiC_6H_5O_7 + 3NH_4OH = Bi(OH)_3 + (NH_4)_3C_6H_5O_7,$$

and this dissolves in the ammonium citrate solution, which is the other product of the reaction, forming a compound which may be called ammonio-bismuth citrate.

The pharmacopœial method of preparation is not altogether satisfactory, and the freshly prepared solution often possesses an opalescence not easily removed by filtration ; but, if set aside for a week, a clear upper layer is obtained which may be siphoned off. On the large scale, the solution is often prepared from bismuth carbonate, with more satisfactory results.

Properties.—A colourless liquid, miscible with water, slightly alkaline to litmus, and having a metallic taste and a slightly ammoniacal odour. It should, preferably, be kept in bottles of lead-free glass.

Quantitative Test.—10 mils, evaporated to dryness, and the residue ignited, should yield not less than 0·5 gramme of bismuth oxide, Bi_2O_3.

BISMUTHI SALICYLAS

Bismuth Salicylate, $C_6H_4(OH).COO(BiO)$. (Mol. Wt. = 361)

Preparation.—Bismuth hydroxide is first prepared by pouring a dilute nitric acid solution of bismuth nitrate into excess of ammonium hydroxide, filtering, washing the precipitate, and drying below 60° :

$$Bi(NO_3)_3 + 3NH_4OH = Bi(OH)_3 + 3NH_4NO_3.$$

The hydroxide is mixed with salicylic acid, water is added, and the

mixture heated nearly to boiling. The amount of salicylic acid employed is such that the liquid shall remain slightly acid. After cooling, the precipitate is filtered off, washed, and dried at a temperature not exceeding 80°:

$$Bi(OH)_3 + C_6H_4(OH).COOH = C_6H_4(OH).COO(BiO) + 2H_2O.$$

The product is a basic salt, the composition of which is somewhat liable to variation. It often retains some free salicylic acid.

Properties.—A white, or nearly white, amorphous powder, tasteless and odourless. Insoluble in water, but is slowly hydrolysed in contact with cold water, more rapidly with hot water, with liberation of salicylic acid, and formation of a more basic salt. It is also partially decomposed by alcohol and by glycerin. When gently heated, it loses salicylic acid, and, on strong ignition, it leaves a residue of bismuth oxide.

Tests for Impurities.—It should be free from impurities described under Bismuthi Carbonas.

Nitrate.—The Pharmacopœia states that it should give not more than the slightest reaction with the copper test (p. 35).

Free Salicylic Acid (Limit of).—Shake 5 grammes with 50 mils of ether, filter, and evaporate the filtrate to dryness. The residue should weigh not more than 0·005 gramme.

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Test.—On ignition it should leave from 62 to 65 per cent of bismuth oxide, Bi_2O_3.

CHAPTER XI

COMPOUNDS OF MERCURY, COPPER, SILVER, AND LEAD

MERCURY AND ITS COMPOUNDS

Hg (Atomic Wt. = 200·5)

THE principal ore of mercury is its sulphide, *cinnabar*, HgS, and from it most of the mercury of commerce is extracted. The free metal sometimes occurs in its ores in the form of minute globules.

Mercury forms two series of salts—the mercurous salts, derived from mercurous oxide, Hg_2O, and the mercuric salts, derived from mercuric oxide, HgO.

General Tests for Mercury.—(1) Many mercury compounds sublime unchanged when heated in a dry tube.

(2) Solutions of mercurous salts yield with dilute hydrochloric acid a white precipitate of mercurous chloride, HgCl. The precipitate is insoluble in boiling water (distinction from lead), and turns black, but does not dissolve, when treated with ammonium hydroxide (distinction from silver).

(3) Solutions of mercuric salts give with hydrogen sulphide a black precipitate of mercuric sulphide, HgS. The precipitate is insoluble in nitric acid, but dissolves in a mixture of concentrated nitric and hydrochloric acids.

(4) A solution of a mercuric salt is reduced by addition of excess of stannous chloride, giving first a white precipitate of mercurous chloride, and later a greyish precipitate of minute globules of metallic mercury.

HYDRARGYRUM

Mercury

Preparation.—(1) Mercury is generally obtained from cinnabar by roasting in a furnace through which passes a current of air :

$$HgS + O_2 = Hg + SO_2.$$

The mercury vapour is condensed in a series of pear-shaped vessels (aludels) made of earthenware.

(2) Another process consists in heating cinnabar with lime in closed retorts :

$$4HgS + 4CaO = 4Hg + CaSO_4 + 3CaS.$$

Mercury obtained by either of these processes is purified by, first, straining through chamois leather to remove dross and dust, and then either distilling from iron retorts or treating with very dilute nitric acid, to remove traces of lead, copper, and other elements. Mercury which has not been freed from these impurities tarnishes in air owing to the formation of their oxides, and, on pouring from a glass vessel, leaves behind a " tail " of oxide or dross.

Properties.—A very heavy, silver-white, liquid metal, readily divisible into globules. Specific gravity, 13·6. It boils at 357°, and solidifies at $-39°$ to form a lead-like mass. On exposure to pure air it remains bright, but in air containing traces of hydrogen sulphide it tarnishes, owing to the production of mercuric sulphide. It is not acted upon by hydrochloric acid ; but it dissolves slowly in concentrated sulphuric acid with evolution of sulphur dioxide and formation of mercuric sulphate :

$$Hg + 2H_2SO_4 = HgSO_4 + SO_2 + 2H_2O.$$

It dissolves in concentrated nitric acid to produce mercurous nitrate, $HgNO_3$, when the liquid is kept cold and the metal is in excess, and mercuric nitrate, $Hg(NO_3)_2$, when the liquid is heated and the acid is in excess.

Many metals, when brought into contact with mercury, form alloys, usually known as amalgams.

Tests for Impurities. *Metallic and other Impurities.*—When heated it should volatilise, leaving no appreciable residue. A simple test for the purity of mercury consists in pouring a little of the sample over a clean glass plate ; the mercury should leave no track on the glass.

Hydrargyrum cum Creta. *Mercury with Chalk. Syn.* Grey Powder.—This is made by triturating 1 part of mercury with 2 parts of prepared chalk in a mortar, until the mixture is uniformly grey and metallic globules are no longer visible. A quicker method consists in placing the mercury in a dry bottle, adding a little ether, allowing the ether to evaporate, then adding the chalk, and shaking until no metallic globules are visible.

Properties.—A light grey powder, free from grittiness, with a tendency to aggregate into minute globules.

Test for Impurity.—When treated with dilute hydrochloric acid, the chalk dissolves, leaving the mercury in a finely divided state. The filtered liquid should yield no white or grey precipitate on the addition of stannous chloride solution (absence of mercuric compounds).

Emplastrum Hydrargyri. *Mercurial Plaster.*—A very small quantity of sulphur is heated with a little olive oil on a sand-bath until a reddish-brown liquid is obtained. Mercury is then triturated with this until metallic globules are no longer visible ; previously melted lead plaster is then added and the mixture triturated until

homogeneous. The division of the mercury is facilitated by the formation of some mercuric sulphide.

Mercury in a finely divided state is also a constituent of Linimentum Hydrargyri, Pilula Hydrargyri, Unguentum Hydrargyri, Unguentum Hydrargyri Compositum.

HYDRARGYRI OXIDUM RUBRUM

Red Mercuric Oxide, HgO. (Mol. Wt. = 216·5.)
Syn. Red Precipitate

This is required to contain not less than 99·3 per cent of HgO.

Preparation.—(1) Red mercuric oxide is slowly formed when mercury is heated to 300° in air.

(2) It may be prepared by dissolving 8 parts by weight of mercury in a mixture of 9 parts of concentrated nitric acid and 2 parts of water:

$$3Hg + 8HNO_3 = 3Hg(NO_3)_2 + 4H_2O + 2NO.$$

The solution of mercuric nitrate is evaporated to dryness, and the residue triturated with 8 parts by weight of mercury until a uniform mixture is obtained. The mixture is heated in a porcelain dish until acid vapours cease to be evolved and the mercurous nitrate, which is at first produced, is converted into mercuric oxide:

$$Hg(NO_3)_2 + Hg = 2HgNO_3,$$
$$HgNO_3 = HgO + NO_2.$$

Properties.—An orange-red powder or crystalline scales. Insoluble in water, but soluble in dilute hydrochloric or nitric acids with formation of the mercuric salt of the acid. When gently heated it becomes dark violet, but turns red again on cooling. When strongly heated in a test-tube it decomposes into oxygen and mercury, the latter forming a sublimate on the cool portions of the tube:

$$2HgO = 2Hg + O_2.$$

Tests for Impurities. *Non-volatile Solids (Limit of).*—When heated to dull redness it should volatilise, leaving not more than 0·3 per cent of residue.

Nitrate.—When gently heated in a test-tube it should not evolve brown fumes.

Quantitative Estimation.—It is estimated by conversion into mercuric nitrate and titration of this with standard ammonium thiocyanate. Mercuric nitrate reacts with ammonium thiocyanate in a similar manner to silver nitrate, producing mercuric thiocyanate, but in the presence of excess of nitric acid the thiocyanate is not immediately precipitated. Weigh about 1 gramme, dis-

solve in 4 mils of nitric acid, and dilute to 100 mils. To portions of 20 mils add a few drops of ferric sulphate solution as indicator, and then titrate with N/10 ammonium thiocyanate until a permanent pink coloration is produced. The coloration is not formed permanently while any of the mercuric nitrate remains in the solution, but when the whole of this has reacted with the thiocyanate, the next drop of the latter added produces a pink coloration owing to the formation of ferric thiocyanate, $Fe(SCN)_3$:

$$HgO + 2HNO_3 = Hg(NO_3)_2 + H_2O,$$
$$Hg(NO_3)_2 + 2NH_4SCN = 2NH_4NO_3 + Hg(SCN)_2,$$
$$2NH_4SCN \equiv Hg(NO_3)_2 \equiv HgO,$$
$$2 \times 76 \equiv 216{\cdot}5 \text{ grammes of } HgO,$$
$$1000 \text{ mils } N/1\ NH_4SCN \equiv 108{\cdot}25 \text{ grammes of } HgO,$$
$$1 \text{ mil } N/10\ NH_4SCN \equiv 0{\cdot}010825 \text{ gramme of } HgO.$$

HYDRARGYRI OXIDUM FLAVUM

Yellow Mercuric Oxide, HgO. (Mol. Wt. = 216·5)

This is required to contain not less than 99·3 per cent of HgO.

Preparation.—The yellow oxide is not formed when mercury or a mercuric salt is heated in air; it is usually prepared by various processes of precipitation, the following being a common method. A warm aqueous solution of 5 parts of mercuric chloride, filtered if necessary, is slowly added to a solution of 2 parts of sodium hydroxide. After stirring well, the yellow precipitate is allowed to subside, washed by decantation, transferred to a calico filter, and again washed until free from chloride. It is then dried at atmospheric temperature.

Properties.—A yellow amorphous powder. Insoluble in water, but readily soluble in mineral acids with formation of the mercuric salt of the acid used. When gently heated it is converted into the red oxide, which then decomposes into mercury and oxygen when the temperature is raised. The yellow oxide differs from the red oxide in physical properties, and, chemically, the yellow oxide is more reactive than the red, the differences being due, presumably, to its finer state of subdivision, or to a difference in molecular complexity.

Tests for Impurities. *Non-volatile Solids (Limit of).*—When treated as under Hydrargyri Oxidum Rubrum it should leave not more than 0·5 per cent of residue.

Free Alkali.—When 1 gramme is shaken with 5 mils of water for five minutes, the mixture should be neutral to litmus.

Quantitative Estimation.—It is estimated in exactly the same manner as Hydrargyri Oxidum Rubrum.

HYDRARGYRI PERCHLORIDUM

Mercuric Chloride, $HgCl_2$. (Mol. Wt. = 271·5)

Syns. Corrosive Sublimate ; Perchloride of Mercury ; Bichloride of Mercury

This is required to contain not less than 98·6 per cent of $HgCl_2$.

Preparation.—(1) It is usually manufactured by heating a mixture of mercuric sulphate, sodium chloride, and a little manganese dioxide, and collecting the sublimate:

$$HgSO_4 + 2NaCl = HgCl_2 + Na_2SO_4.$$

The manganese dioxide—an oxidising agent—prevents the formation of mercurous chloride.

(2) It is sometimes obtained by passing chlorine over metallic mercury, heated nearly to boiling:

$$Hg + Cl_2 = HgCl_2.$$

Properties.—Heavy, colourless, crystalline masses, or needle-shaped crystals. Soluble 1-18 in water, 1-4 in alcohol (90 per cent), and 1-4 in ether. When heated, it sublimes without decomposition, and should leave not more than a trace of residue.

Quantitative Estimation.—It is estimated by reducing to metallic mercury and weighing. Weigh about 0·5 gramme, dissolve in 20 mils of water in a tared beaker-flask. Add sufficient hypophosphorous acid (about 10 mils) to reduce the whole of the mercuric chloride, and heat on a water-bath until the mercury collects at the bottom of the flask. Decant the supernatant liquid through a tared filter-paper, in order to avoid loss of mercury, and wash the flask successively with water, alcohol (90 per cent), and ether, passing the washings through the filter-paper. Dry both flask and filter-paper over concentrated sulphuric acid in a desiccator, and weigh :

$$Hg \equiv HgCl_2,$$
$$200·5 \text{ grammes} \equiv 271·5 \text{ grammes}.$$

The Pharmacopœia requires that mercuric chloride shall yield between 72·8 and 73·8 per cent of metallic mercury.

Liquor Hydrargyri Perchloridi. *Solution of Mercuric Chloride.*—This is a 0·1 per cent *w/v* solution of mercuric chloride ; it should be kept protected from light, as otherwise it may lose strength through deposition of mercurous chloride, HgCl.

HYDRARGYRUM AMMONIATUM

Ammoniated Mercury, NH_2HgCl. (Mol. Wt. = 252)

Syns. White Precipitate ; Ammonio-chloride of Mercury Mercuric-ammonium Chloride

This is required to contain not less than 94·5 per cent of NH_2HgCl

It may be regarded as ammonium chloride, NH_4Cl, in which

two atoms of hydrogen have been displaced by an atom of mercury.

Preparation.—A solution of 3 parts of mercuric chloride in 60 parts of water is added, with constant stirring, to 4 parts of Solution of Ammonia, diluted with 20 parts of water:

$$HgCl_2 + 2NH_3 = NH_2HgCl + NH_4Cl.$$

The precipitate is collected on a filter, washed with cold water, and dried at a temperature not exceeding 30°. The washing should not be continued long enough to remove all the ammonium chloride, or the product will be yellowish.

Properties.—A heavy, white, amorphous powder, insoluble in water, alcohol, and ether. It is slowly decomposed by cold water, and boiling water converts it into a yellow basic compound, NH_2HgCl,HgO. Warmed with sodium hydroxide solution, it evolves ammonia and becomes yellow, and the liquid, filtered and acidified with nitric acid, yields a white precipitate of silver chloride on addition of silver nitrate. On heating, it should sublime without appreciable residue.

Quantitative Estimation.—It is estimated by adding excess of potassium iodide and titrating the liberated ammonium and potassium hydroxides with standard acid:

$$NH_2HgCl + 2KI + 2H_2O = HgI_2 + NH_4OH + KOH + KCl.$$

The mercuric iodide dissolves in the excess of potassium iodide. Weigh 0·3 gramme, triturate in a glass mortar with a few drops of water, and transfer to a flask with the aid of 40 mils of water; then rinse the mortar with a solution of about 2 grammes of potassium iodide in 10 mils of water, add this to the contents of the flask, cork the flask, and shake until solution is complete. Titrate with N/10 hydrochloric acid, using methyl orange as indicator:

$$NH_2HgCl \equiv NH_4OH + KOH,$$
$$2HCl + NH_4OH + KOH = NH_4Cl + KCl + 2H_2O,$$
$$2HCl \equiv NH_2HgCl,$$
$$2 \times 36{\cdot}5 \equiv 252.$$
$$1000 \text{ mils N/1 HCl} \equiv 126 \text{ grammes of } NH_2HgCl,$$
$$1 \text{ mil N/10 HCl} \equiv 0{\cdot}0126 \text{ gramme of } NH_2HgCl.$$

HYDRARGYRI IODIDUM RUBRUM

Red Mercuric Iodide, HgI_2. (Mol. Wt. = 454·5.)
Syns. Biniodide of Mercury; Mercuric Iodide

Preparation.—This is made by mixing dilute solutions of mercuric chloride (4 parts) and potassium iodide (5 parts), collecting the precipitate, washing with cold water, and drying below 40°:

$$HgCl_2 + 2KI = HgI_2 + 2KCl.$$

Properties.—A bright, scarlet-red, minutely crystalline powder. Almost insoluble in water; sparingly soluble in alcohol (90 per cent); readily soluble in ether. It is freely soluble in aqueous solutions of potassium iodide and other iodides owing to the formation of soluble double salts. When heated, it becomes yellow at 150°, and, at higher temperatures, volatilises.

Tests for Impurities. *Non-volatile Solids.*—When heated to dull redness it should volatilise, leaving not more than a trace of residue.

Mercurous Iodide.—It should be freely and entirely soluble in ether.

Mercuric and other Chlorides (Limit of).—Shake 0·5 gramme with 10 mils of water, and filter. The filtrate should not be coloured more than slightly brown by hydrogen sulphide (limit of mercuric chloride), and should not become more than opalescent on addition of silver nitrate (limit of chlorides).

LIQUOR HYDRARGYRI NITRATIS ACIDUS

Acid Solution of Mercuric Nitrate

Preparation.—Mercury (24 parts by weight) is dissolved in a mixture of 30 parts of nitric acid and 9 parts of water, without the aid of heat, in a tared flask:

$$2Hg + 2HNO_3 = HgNO_3 + 2H,$$
$$HNO_3 + 2H = HNO_2 + H_2O..$$

The solution of mercurous nitrate is green owing to the presence of nitrous acid. When all the mercury has dissolved, the solution is boiled, mercuric nitrate being formed, and oxides of nitrogen evolved:

$$HgNO_3 + 2HNO_3 = Hg(NO_3)_2 + H_2O + NO_2.$$

The liquid is then evaporated to 72 parts by weight. If heating be commenced before all the mercury has dissolved, a violent reaction takes place.

Properties.—A colourless, strongly acid liquid. Specific gravity about 2·0. It should be preserved in a stoppered bottle away from light.

Test for Impurity.—On diluting and adding dilute hydrochloric acid there should be no precipitate (absence of mercurous salts).

Unguentum Hydrargyri Nitratis. *Mercuric Nitrate Ointment.*—This is prepared by dissolving mercury in cold nitric acid, and gradually adding the solution of mercurous nitrate to a mixture of lard and olive oil, previously heated on a sand-bath to 150° and transferred to an earthenware jar. The mixture is stirred constantly at a temperature of not less than 90° until oxides of nitrogen cease to be evolved, and then stirred until cold.

The heat converts the mercurous nitrate into mercuric nitrate:

$$HgNO_3 + 2HNO_3 = Hg(NO_3)_2 + H_2O + NO_2,$$

and by the action of the excess of nitric acid, the tri-olein (p. 274) of the lard and olive oil is converted into its isomer eläidin.

HYDRARGYRI SUBCHLORIDUM

Mercurous Chloride, $HgCl$. (Mol. Wt. = 236.)
Syns. Calomel; Subchloride of Mercury; Hydrargyri Chloridum

Preparation.—(1) This is obtained as a sublimate by heating an intimate mixture of mercuric sulphate, mercury, and sodium chloride:

$$HgSO_4 + Hg = Hg_2SO_4,$$
$$Hg_2SO_4 + 2NaCl = 2HgCl + Na_2SO_4.$$

The product is repeatedly washed, first with dilute nitric acid to remove traces of free mercury, and then with water, to remove soluble mercuric salts.

(2) It is also obtained when an intimate mixture of mercuric chloride and mercury is sublimed:

$$HgCl_2 + Hg = 2HgCl.$$

Properties.—A heavy, white, or slightly yellowish powder, nearly tasteless. Insoluble in water, alcohol, ether, and dilute acids. A hot mixture of concentrated nitric and hydrochloric acids oxidises it to soluble mercuric chloride. Treated with sodium, potassium, ammonium, or calcium hydroxides it becomes black (*vide infra*). When heated, it sublimes.

Tests for Impurities. *Non-volatile Solids.*—When strongly heated it should leave not more than a trace of residue.

Mercuric-ammonium Chloride.—When warmed with sodium hydroxide solution, no ammonia should be evolved (test with turmeric paper, p. 32).

Mercuric Chloride.—Shake 1 gramme with 10 mils of water and filter. The filtrate should not be darkened by hydrogen sulphide. Owing to the highly toxic nature of mercuric chloride, this is a very important test.

MERCURIAL LOTIONS

Lotio Hydrargyri Flava. *Yellow Mercurial Lotion.* *Syn.* Yellow Wash.—This is prepared by adding 4·6 parts of mercuric chloride to 1000 parts of Solution of Lime. The resulting precipitate is one of yellow oxide of mercury:

$$Ca(OH)_2 + HgCl_2 = CaCl_2 + HgO + H_2O.$$

It is always advisable to add the salt to the lime water, and not *vice versa*, or there is a possibility of the red oxide being produced.

Lotio Hydrargyri Nigra. *Black Mercurial Lotion.* *Syn.* Black Wash.—This is prepared by triturating 6·85 parts of mercurous

chloride with 50 parts of glycerin, and adding sufficient Solution of Lime to produce 1000 parts.

The black precipitate consists in the first instance of mercurous oxide:

$$Ca(OH)_2 + 2HgCl = Hg_2O + CaCl_2 + H_2O,$$

but on exposure to light the precipitate becomes brownish, owing to partial decomposition into mercury and mercuric oxide:

$$Hg_2O = HgO + Hg.$$

COMPOUNDS OF COPPER

Cu (Atomic Wt. = 63·5)

Copper is sometimes found in Nature in the free state, but is generally extracted from the mineral *copper pyrites*, $CuFeS_2$. Of the many copper ores of lesser importance may be mentioned *cuprite*, Cu_2O, *copper glance*, Cu_2S, and *malachite*, $CuCO_3,Cu(OH)_2$.

Copper forms two series of salts—the cuprous salts, derived from cuprous oxide, Cu_2O, and the cupric salts, derived from cupric oxide, CuO. Most salts of copper are blue or green. Only one—cupric sulphate—is official.

General Tests for Copper.—(1) Hydrogen sulphide gives with solutions of copper salts a black precipitate of cupric sulphide, CuS. The precipitate is insoluble in yellow ammonium sulphide, but dissolves in dilute nitric acid on boiling.

(2) Ammonium hydroxide, added to a solution of a copper salt, produces a pale blue precipitate of cupric hydroxide, $Cu(OH)_2$, which dissolves in excess of the precipitant to form a deep blue solution, containing a complex ammine, of the type $Cu(NH_3)_4SO_4$.

(3) A solution of a copper salt, acidified with acetic acid, gives with potassium ferrocyanide a brown precipitate of copper ferrocyanide. This is a very delicate test for copper. Even with minute traces a brown coloration is produced.

(4) Copper compounds, moistened with strong hydrochloric acid, impart a green colour to the bunsen flame.

CUPRI SULPHAS

Copper Sulphate, $CuSO_4,5H_2O$. (Mol. Wt. = 249·5.)
Syn. Cupric Sulphate. *Unofficial Syn.* Blue Vitriol

Preparation.—(1) It may be prepared by heating cupric oxide with dilute sulphuric acid, or metallic copper with concentrated sulphuric acid:

$$CuO + H_2SO_4 = CuSO_4 + H_2O,$$
$$Cu + 2H_2SO_4 = CuSO_4 + SO_2 + 2H_2O.$$

(2) It is manufactured on the large scale by heating scrap copper with dilute sulphuric acid, a current of air being passed through the liquid:

$$2Cu + 2H_2SO_4 + O_2 = 2CuSO_4 + 2H_2O.$$

The product in all these cases is purified by crystallisation from water.

Properties.—Blue triclinic prisms. Soluble 1·3·5 in water, forming an acid solution owing to hydrolysis; very soluble in glycerin, almost insoluble in alcohol (90 per cent). When heated to 100°, it loses 4 molecules of water of crystallisation, and at about 250° it becomes anhydrous, the anhydrous salt being white, but becoming blue again on moistening with water. Copper sulphate liberates iodine from a solution of potassium iodide acidified with acetic acid:

$$CuSO_4 + 2KI = CuI_2 + K_2SO_4,$$
$$2CuI_2 = 2CuI + I_2.$$

This reaction is sometimes employed in the quantitative estimation of copper sulphate, the liberated iodine being titrated with standard thiosulphate solution.

Tests for Impurities. (To be applied to the aqueous solution.) *Lead.*—Boil with excess of sodium hydroxide solution, and filter. Add to the filtrate ammonium hydroxide and potassium cyanide, then a drop of sodium sulphide solution, when there should be no dark coloration.

Iron (Limit of).—Weigh 5 grammes, dissolve in about 25 mils of water, add 2 mils of concentrated nitric acid, heat to boiling, cool, and add strong ammonium hydroxide until the precipitate which first forms is redissolved and the liquid has a distinct odour of ammonia. Filter, wash the filter-paper thoroughly with very dilute ammonium hydroxide, redissolve in hydrochloric acid any precipitate that has been collected, reprecipitate with ammonium hydroxide, collect, wash, dry, ignite, and weigh the residue. It should not weigh more than 0·007 gramme, corresponding to less than 0·1 per cent of iron, calculated as Fe, in the sample of copper sulphate.

Aluminium and Zinc.—Add a few drops of dilute hydrochloric acid and pass hydrogen sulphide to precipitate all the copper. Filter, boil the filtrate to expel hydrogen sulphide, add a few drops of nitric acid, and again boil. Add excess of sodium hydroxide, filter if necessary, add to the filtrate excess of ammonium chloride, and boil. There should be no precipitate (absence of aluminium). Filter, and pass hydrogen sulphide through the filtrate, when there should be no precipitate (absence of zinc).

Arsenic Limit.—10 parts per million (p. 176).

COMPOUNDS OF SILVER

Ag (Atomic Wt. = 108)

Silver occurs in the free state and also as *silver glance*, Ag_2S; many silver ores consist of the sulphide associated with the sulphides of arsenic, antimony, or copper. Much of the silver of commerce is obtained from *galena* (p. 167), which contains notable quantities of silver compounds.

General Tests for Silver.—(1) Hydrochloric acid added to a solution of a silver salt gives a white precipitate of silver chloride, AgCl, insoluble in nitric acid and in boiling water, but soluble in ammonium hydroxide (distinction from mercurous salts and lead).

(2) Potassium chromate, added to a neutral solution of a silver salt, gives a red precipitate of the chromate, Ag_2CrO_4, soluble in dilute nitric acid.

ARGENTI NITRAS

Silver Nitrate, $AgNO_3$. (Mol. Wt. = 170.) *Syn.* Lunar Caustic

Preparation.—Metallic silver is dissolved in hot, fairly concentrated nitric acid:

$$Ag + 2HNO_3 = AgNO_3 + H_2O + NO_2.$$

The solution is evaporated to dryness, and the residue heated to expel all nitric acid. The product is then purified by recrystallisation from water.

Properties.—Colourless tabular crystals, with a bitter, caustic metallic taste. Soluble 2·1 in water, forming a neutral solution; slightly soluble in alcohol (90 per cent). It melts at about 218° without decomposition, but decomposes at a red heat with evolution of oxides of nitrogen, leaving a residue of metallic silver.

Tests for Impurities. *Lead.*—The aqueous solution should give no turbidity on adding dilute sulphuric acid and warming. Minute traces of lead may be detected by adding excess of hydrochloric acid to an aqueous solution, filtering, rendering the filtrate alkaline with ammonium hydroxide, and adding potassium cyanide followed by a drop of sodium sulphide solution, when there should be no dark coloration.

Copper.—Add to the aqueous solution excess of ammonium hydroxide, and filter. The filtrate should have no blue tinge, and on acidifying with acetic acid and adding potassium ferrocyanide the precipitate produced should be white, with no brown tinge.

Iron.—Acidify the aqueous solution with nitric acid, and add potassium ferrocyanide, when there should be no blue or green coloration.

Sulphate.—Add excess of hydrochloric acid to a solution, and filter. The filtrate should give no turbidity on the addition of barium chloride.

Quantitative Estimation.—It is estimated gravimetrically as the chloride, AgCl. Weigh about 0·5 gramme, dissolve in about 50 mils of hot water, and add a slight excess of hydrochloric acid. Boil, collect the precipitate on asbestos in a tared Gooch crucible; wash until the washings are free from chloride; dry the crucible and contents in an air-oven at about 120°, cool, and weigh:

$$AgNO_3 + HCl = AgCl + HNO_3,$$
$$AgCl \equiv AgNO_3,$$
$$143\cdot5 \text{ grammes} \equiv 170 \text{ grammes}.$$

The Pharmacopœia requires that from 1 gramme of silver nitrate the precipitate shall weigh 0·843 gramme.

Argenti Nitras Induratus. *Toughened Caustic.*—This is prepared by melting 19 parts of silver nitrate and 1 part of potassium nitrate in a porcelain dish, mixing well, and pouring the fused mass into cylindrical or conical moulds of silver or platinum.

Properties.—White or greyish-white, cylindrical rods or cones which are much less brittle than pure silver nitrate. Very caustic. Freely soluble in water; sparingly soluble in alcohol (90 per cent).

Quantitative Estimation.—The silver is estimated as chloride, as described under Argenti Nitras, using the same quantity. The Pharmacopœia requires that the precipitate obtained from 1 gramme shall weigh 0·8 gramme and that the filtrate, on evaporation, shall yield a white residue.

Argenti Nitras Mitigatus. *Mitigated Caustic.*—This is prepared in the same manner as Argenti Nitras Induratus, except that only 1 part of silver nitrate is employed to 2 parts of potassium nitrate. It is similar in properties, but is less caustic.

Quantitative Estimation.—As for Argenti Nitras, using about 1·5 gramme of the substance. The Pharmacopœia requires that the precipitate from 3 grammes shall weigh 0·843 gramme.

COMPOUNDS OF LEAD

Pb (Atomic Wt. = 207)

Lead is nearly always obtained from the naturally occurring sulphide, *galena*, PbS. Other lead ores are *cerussite*, $PbCO_3$, and *anglesite*, $PbSO_4$. The metal is obtained from galena by roasting in a reverberatory furnace. The first reaction is the oxidation of part of the sulphide to a mixture of sulphate and oxide:

$$PbS + 2O_2 = PbSO_4,$$
$$2PbS + 3O_2 = 2PbO + 2SO_2.$$

On raising the temperature, the sulphate and oxide react with the rest of the sulphide, and the metal is liberated:

$$PbSO_4 + PbS = 2Pb + 2SO_2,$$
$$2PbO + PbS = 3Pb + SO_2.$$

Lead forms a number of oxides, of which three—litharge, PbO (yellow), lead peroxide, PbO_2 (brown), and "red lead", Pb_3O_4 (red)—are the most important. The stable salts of lead are derived from litharge.

General Tests for Lead.—(1) When heated with sodium carbonate on a charcoal block in the blowpipe flame, lead compounds yield a bead of metal and a yellow encrustation of oxide. The metallic bead is soft and malleable, and marks paper.

(2) A cold solution of a lead salt gives, with hydrochloric acid, a white precipitate of the chloride, $PbCl_2$. The precipitate is soluble in hot water and crystallises out in small needles on cooling.

(3) Potassium chromate gives with solutions of lead salts a yellow precipitate of lead chromate, $PbCrO_4$, insoluble in acetic acid.

(4) Hydrogen sulphide precipitates black lead sulphide, PbS, when passed through solutions of lead salts. The precipitate is insoluble in dilute hydrochloric acid, but is soluble in boiling dilute nitric acid. If only traces of lead are present in a solution, hydrogen sulphide produces a brown coloration.

(5) Sulphuric acid precipitates lead sulphate, $PbSO_4$, from solutions of lead salts. The precipitate is almost insoluble in water, and even less soluble in dilute alcohol.

PLUMBI OXIDUM

Lead Oxide, PbO. (Mol. Wt. = 223.) *Syn.* Litharge

Preparation.—(1) Litharge is formed when lead nitrate or carbonate is heated:

$$2Pb(NO_3)_2 = 2PbO + 4NO_2 + O_2.$$

(2) It is manufactured by allowing a powerful air-blast to impinge upon molten lead. The air-blast causes the oxidation of the metal, and partially separates the comparatively light surface film of oxide from the heavy metal:

$$2Pb + O_2 = 2PbO.$$

Litharge is generally obtained in this way during the extraction of silver from argentiferous lead ores (p. 166). When the oxide is prepared at a fairly low temperature it forms a yellow, amorphous powder known as massicot, which is changed into litharge by fusing and allowing to cool.

Properties.—Heavy, reddish-yellow, semi-crystalline scales, or a reddish-yellow powder. Almost insoluble in water. Wh...

heated, it changes in colour to dark reddish-brown, becoming yellow again on cooling. It melts at a bright red heat without decomposition. It dissolves in acids with formation of the salt of the acid used.

Tests for Impurities. *Carbonate and Silica.*—It should dissolve in dilute nitric acid, and in acetic acid, with but slight effervescence, leaving not more than traces of insoluble residue.

Copper.—Dissolve in dilute nitric acid, add excess of ammonium hydroxide and filter. The filtrate should have no blue tinge, and on acidifying with acetic acid and adding potassium ferrocyanide should not acquire a brown coloration.

Iron.—Dissolve in dilute nitric acid and add potassium ferrocyanide, when there should not be more than a slight blue or green colour

PLUMBI IODIDUM

Lead Iodide, PbI_2. (Mol. Wt. = 461)

Preparation.—Add a solution of 9 parts of lead acetate in 40 parts of boiling water to one of 8 parts of potassium iodide in 5 parts of boiling water. On cooling, lead iodide crystallises out, and is collected on a filter, washed with cold water and dried on a porous plate :

$$(CH_3.COO)_2Pb + 2KI = PbI_2 + 2CH_3.COOK.$$

Instead of lead acetate, 8 parts of lead nitrate may be employed.

Properties.—Very small, slender, glistening, golden-yellow crystals. Samples which have been prepared by precipitation from cold solutions, and not subsequently crystallised, are met with as a heavy, bright yellow powder. Soluble 1-2000 in cold water, 1-200 in boiling water, forming colourless, neutral solutions. A hot saturated solution, on cooling, deposits the salt in golden-yellow crystals, the appearance of which is very characteristic. It is readily soluble in ammonium chloride solution. On heating in air, it darkens until almost black, and at higher temperatures it is oxidised with loss of iodine, a yellow crystalline basic iodide remaining.

Tests for Impurities. *Chromate and other Insoluble Salts.*—It should be completely soluble when heated on a water-bath with a strong solution of ammonium chloride.

Nitrate.—Boil with water, cool, and filter. To the filtrate add dilute sulphuric acid, a scrap of zinc, and some starch mucilage. No blue colour should develop.

Acetate.—Boil with water, cool, filter, pass hydrogen sulphide through the filtrate to completely precipitate the lead, and filter again. Boil the filtrate to expel hydrogen sulphide ; cool, carefully neutralise with ammonium hydroxide, and add a drop of ferric chloride solution. There should be no red coloration.

PLUMBI ACETAS

Lead Acetate $(CH_3.COO)_2Pb,3H_2O$. (Mol. Wt. = 379)
Syn. Sugar of Lead

This is required to contain not less than 99·5 per cent of $(CH_3.COO)_2Pb,3H_2O$.

Preparation.—It may be prepared in the laboratory by boiling 1 part of litharge with 2 parts of 30 per cent acetic acid, filtering while hot, and allowing to cool:

$$PbO + 2CH_3.COOH = (CH_3.COO)_2Pb + H_2O.$$

The crystals are collected, and dried at atmospheric temperature. Lead carbonate may be employed instead of the oxide.

On the large scale, vapours of acetic acid are passed through vessels containing perforated shelves on which the litharge is spread.

Properties.—Colourless, monoclinic prisms, or white crystalline masses, slightly efflorescent. It has a sweet though astringent taste, and a slight odour of acetic acid, the odour being due to its slow decomposition into acetic acid and a basic acetate. Soluble 1-2·5 in water, forming an acid solution which is clear, or, if slightly turbid, becomes clear on addition of acetic acid. Soluble 1-30 in alcohol (90 per cent). When heated to 40°, or even when left in a desiccator over sulphuric acid, it loses its water of crystallisation. When heated rapidly, the crystalline salt dissolves in its water of crystallisation, and as the temperature is raised, it is converted into a basic salt, with loss of acetic acid. On continued heating, inflammable vapours are evolved, and eventually there remains a yellowish residue consisting of finely divided lead mixed with oxide.

Tests for Impurities. *Silver.*—Add a few drops of hydrochloric acid to an aqueous solution, and heat to boiling, when the solution should be clear.

Arsenic.—Apply Fleitmann's test (p. 143).

Copper and Iron.—Test as under Plumbi Oxidum.

Zinc and Calcium.—To the aqueous solution add a slight excess of dilute hydrochloric acid; cool well, filter, pass hydrogen sulphide through the filtrate to complete the removal of the lead, and again filter. Boil the filtrate to expel hydrogen sulphide, add a few drops of nitric acid, and boil again; then add ammonium chloride and excess of ammonium hydroxide, and filter if necessary. Pass hydrogen sulphide through the filtrate, when there should be no precipitate (absence of zinc). Filter, boil, then add to the filtrate ammonium oxalate, when there should be no precipitate (absence of calcium).

Carbonate.—The aqueous solution, prepared with previously boiled and cooled water, should not be more than slightly opalescent.

Chloride.—Acidify the aqueous solution with nitric acid and add silver nitrate. There should be no opalescence.

Nitrate.—Apply the brown ring test (p. 35).

Quantitative Estimation.—The lead is estimated by precipitation as oxalate from an acetic acid solution, the precipitate being heated with sulphuric acid, and the liberated oxalic acid titrated with standard potassium permanganate. Weigh 0·5 gramme, dissolve in water acidified with acetic acid, and add excess of oxalic acid solution. Collect the precipitate on a filter-paper, wash thoroughly to remove excess of oxalic acid, transfer to a flask, add excess of dilute sulphuric acid, warm, and titrate with N/10 potassium permanganate:

$$(CH_3 . COO)_2Pb + (COOH)_2 = (COO)_2Pb + 2CH_3 . COOH,$$
$$(COO)_2Pb + H_2SO_4 = PbSO_4 + (COOH)_2,$$
$$2KMnO_4 + 5(COOH)_2 + 3H_2SO_4 = K_2SO_4 + 2MnSO_4 + 10CO_2 + 8H_2O,$$
$$2KMnO_4 \equiv 5(COOH)_2 \equiv 5(COO)_2Pb \equiv 5(CH_3 . COO)_2Pb,3H_2O,$$
$$2KMnO_4 \equiv 5 \times 379 \text{ grammes of } (CH_3 . COO)_2Pb,3H_2O,$$
$$1000 \text{ mils of N/1 } KMnO_4 \equiv \frac{5 \times 379}{10}$$
$$= 189{\cdot}5 \text{ grammes of } (CH_3 . COO)_2Pb,3H_2O,$$
$$1 \text{ mil N/10 } KMnO_4 \equiv 0{\cdot}01895 \text{ gramme of } (CH_3 . COO)_2Pb,3H_2O.$$

Liquor Plumbi Subacetatis Fortis. *Strong Solution of Lead Subacetate.* *Syn.* Goulard's Extract.

Preparation.—Lead oxide (35 parts) is added to a solution of lead acetate (50 parts) in 150 parts of water, and the mixture set aside for forty-eight hours, with occasional shaking:

$$(CH_3 . COO)_2Pb + PbO + H_2O = (CH_3 . COO)_2Pb,Pb(OH)_2.$$

The solution of basic lead acetate (subacetate) is filtered from the insoluble, more basic acetates which are also formed, and sufficient water passed through the filter, if necessary, to produce a solution of the required specific gravity, using a hydrometer. It may be noted that, since the solution is to have a definite specific gravity, it is useless to adjust it to volume.

Properties.—A clear colourless liquid, with a sweet astringent taste; alkaline to litmus. On exposure to air it becomes turbid, owing to absorption of atmospheric carbon dioxide with precipitation of a basic carbonate:

$$(CH_3 . COO)_2Pb,Pb(OH)_2 + CO_2 + H_2O = PbCO_3,Pb(OH)_2 + 2CH_3 . COOH.$$

Specific gravity 1·275. With mucilage of acacia, the solution yields a thick, white, gelatinous precipitate, which serves to distinguish the solution from one of lead acetate. (This test may also be employed for distinguishing mucilage of acacia from mucilages of other gums.)

Quantitative Estimation.—The lead is estimated as described

under Plumbi Acetas, weighing about 1 gramme of the liquor, and diluting with water. The Pharmacopœia requires that the lead oxalate from 1 gramme of the liquor, after decomposition with sulphuric acid, shall require not less than 17 mils of N/10 potassium permanganate solution.

Liquor Plumbi Subacetatis Dilutus. *Diluted Solution of Lead Subacetate. Syns.* Goulard's Lotion; Goulard Water.—This is a dilution of 12·5 parts of the strong solution to 1000 parts, with previously boiled and cooled water. The use of water containing carbon dioxide would result in the precipitation of some of the lead as basic carbonate.

CHAPTER XII

THE LIMIT-TESTS FOR LEAD AND ARSENIC

LEAD and arsenic in small quantities are frequently present in chemical substances, and such traces are removable only with great difficulty. Owing to the toxicity and cumulative nature of these impurities, it will be seen that their presence in medicinal chemicals is a matter of considerable importance, and this fact received recognition in the 1914 edition of the Pharmacopœia. Although it is not feasible to insist upon the complete absence of lead and arsenic from all medicinal substances, limits are prescribed, varying according to the normal dose of the substance under examination, and, to some extent, to the practicability of preparing ordinary samples containing these impurities in sufficiently small proportions.

The prescribed limits are so small that the ordinary methods of quantitative analysis are useless, and, therefore, special forms of procedure are included in the Pharmacopœia. These will now be described.

THE LIMIT-TEST FOR LEAD

Solutions containing lead salts yield, with sodium sulphide, a black precipitate of lead sulphide, which produces, in very dilute solutions, a brown coloration of varying intensity, according to the quantity of lead salt present. The production of this coloration forms the basis of a colorimetric method described in the Pharmacopœia for the estimation of traces of lead. Under ordinary circumstances, similar precipitates of the sulphides of copper and iron are produced by sodium sulphide, should traces of these metals be present in the solution, and unless suitable precautions are taken to prevent the precipitation of the sulphides of these metals, the lead test is valueless. This difficulty is overcome by previously adding ammonium hydroxide and potassium cyanide, which prevent the precipitation of traces of copper and iron as sulphides.

Two solutions of the substance to be tested are prepared:

(i.) A *primary solution*, containing 12 grammes of the substance and*

(ii.) An *auxiliary solution*, containing 2 grammes of the substance.

* In some cases the primary solution contains 7 or 4 grammes.

To each is added a definite quantity of ammonium hydroxide and of potassium cyanide solution. Sufficient lead nitrate solution of known strength is then added to the auxiliary solution, so that on the addition of sodium sulphide, and dilution to equal volumes, the intensity of the coloration in each solution is the same. By carrying out several comparative tests, adding different quantities of the standard lead nitrate solution to the auxiliary solution for each test, it is possible to determine the parts per million of lead present in the substance. The standard lead solution employed is of such a strength that it contains 10 parts per million of lead, so, since the primary solution contains 10 grammes more of the substance than the auxiliary, it follows that, if the addition of 1 mil of lead solution to the auxiliary solution produces a coloration equal in intensity to that of the primary solution (when sodium sulphide is added to both), then the substance contains 1 part per million of lead.

Apparatus Required

The apparatus employed consists of two Nessler glasses. These are cylindrical vessels made of thin, lead-free glass. They are about 15 centimetres in height, and at a distance of 10 centimetres from the bottom they bear a mark indicating a volume of 50 mils. When the test is being carried out, these glasses are placed close together on a white tile, preferably one of opal glass, and the colorations are viewed by the light reflected from the tile, through the Nessler glasses, at an angle to the observer.

Reagents Required

*Strong Solution of Lead PbT.**—Dissolve 0·16 gramme of lead nitrate in water, add 50 mils of Acidum Nitricum, and dilute to 100 mils. The solution contains 0·001 gramme of lead in 1 mil.

Dilute Solution of Lead PbT.—Dilute 1 mil of the strong solution, measured from a burette, with water to 100 mils. The solution contains 0·00001 gramme of lead in 1 mil.

Solution of Potassium Cyanide PbT.—Dissolve 10 grammes of potassium cyanide in water and add 2 mils of Solution of Hydrogen Peroxide, then dilute the whole to 100 mils. After being allowed to stand, this solution should give no colour with the dilute solution of lead PbT when tested by the limit-test.

Solution of Sodium Sulphide PbT.—Dissolve 10 grammes of sodium sulphide in water and dilute to 100 mils.

General Method of Testing

A primary solution containing 12 grammes of the substance to be tested, and an auxiliary solution containing 2 grammes, are

* The special reagents and solutions used in the limit-test for lead are distinguished by the letters "PbT".

prepared, and filtered if necessary. The solutions are introduced one into each Nessler glass, made alkaline with Solution of Ammonia, and 1 mil of solution of potassium cyanide PbT is added to each. If the colours of the solutions differ much, the difference may be rectified by the very cautious addition of an extremely dilute solution of burnt sugar. The volume of the primary solution is then adjusted to the 50-mil mark, and 2 drops of sodium sulphide solution PbT added.

The next step is to ascertain what volume of dilute solution of lead PbT (in mils, measured from a burette) it is necessary to add to the auxiliary solution so that its colour (after dilution to 50 mils and the addition of 2 drops of sodium sulphide solution PbT) shall be the same as that of the primary solution. This can only be ascertained by a series of experiments, and the first step is to use the maximum quantity permissible, since if this fails to produce sufficient coloration in the auxiliary solution, the substance contains more lead than is allowed by the official limit.

For example, say that the substance under examination is Acidum Hydrochloricum, then not more than 10 mils of dilute solution of lead PbT should be required to produce a coloration in the auxiliary solution equal to that in the primary solution.

In some cases, 7 grammes of the substance are used in the primary solution, when each mil of dilute solution of lead PbT will correspond to 2 parts per million of lead. In other cases, only 4 grammes of the substances are used in the primary solution, when each mil of dilute solution of lead PbT will correspond to 5 parts per million of lead.

List of Substances

Primary Solution, 12 *grammes: Auxiliary Solution,* 2 *grammes.*

(Figures in brackets indicate limit of lead in parts per million.)

Acidum Hydrobromicum (5).
Acidum Hydrochloricum (10).
Acidum Phosphoricum Conc. (10).
Acidum Sulphurosum (10).
Ammonii Bromidum (10).
[1] Ammonii Carbonas (5).
Ammonii Chloridum (5).
Lithii Citras (5).
Magnesii Sulphas (5).
Potassii Acetas (10).
Potassii Bicarbonas (5).
Potassii Bromidum (10).
Potassii Carbonas (5).
Potassii Citras (10).
Potassii Iodidum (10).
Potassii Nitras (10).
Sodii Bromidum (10).
Sodii Carbonas (10).
Sodii Chloridum (10).
Sodii Iodidum (10).
Sodii Phosphas (5).
Sodii Phosphas Acidus (5).
Sodii Salicylas (10).
Sodii Sulphas (5).

Primary Solution, 7 grammes: Auxiliary Solution, 2 grammes.

[2] Acidum Acetylsalicylicum (10).	[4] Calcii Lactas (10).
[2] Acidum Boricum (25).	[3] Lithii Carbonas (10).
Acidum Citricum (20).	[3] Mag. Carb. Levis (20).
Acidum Hydriodicum Dil. (10).	[3] Mag. Carb. Pond. (20).
Acidum Lacticum (10).	Potassii Chloras (10).
Acidum Nitricum (20).	Potassii Sulphas (20).
Acidum Sulphuricum (20).	Potassii Tartras (20).
Acidum Tartaricum (20).	[2] Potass. Tart. Acid. (20).
Ammonii Benzoas (10).	Sodii Benzoas (10).
Borax Purificatus (5).	[5] Sodii Bicarbonas (5).
[3] Calc. Carb. Præcip. (10).	Sodii Carb. Exsic. (25).
[4] Calcii Chloridum (20).	Sod. et. Pot. Tart. (20).
[3] Calcii Hydras (20).	Sodii Hypophosphis (10).
[4] Calcii Hypophosphis (10).	[4] Strontii Bromidum (20).

Primary Solution, 4 grammes: Auxiliary Solution, 2 grammes.

[3] Magnesia Levis (20).
[3] Magnesia Ponderosa (20).

Liquor Magnesii Bicarbonatis (0·5).—The primary solution is prepared by treating 200 mils with excess of acetic acid and concentrating so that the solution (after being made alkaline with Solution of Ammonia, and treated with solution of potassium cyanide PbT) measures 50 mils. Auxiliary solution consists of 100 mils similarly treated.

Notes:
[1] Primary solution boiled down to measure 50 mils.
[2] Solution is effected by the addition of Solution of Ammonia.
[3] Solution prepared by dissolving in excess of Acidum Aceticum, boiling to expel any carbon dioxide present, then making alkaline with Solution of Ammonia, and adding solution of potassium cyanide PbT.
[4] Acetic acid added to each solution before making alkaline with Solution of Ammonia.
[5] Solution is effected by boiling.

THE ARSENIC LIMIT-TEST *

This test depends upon the fact that when hydrogen is produced by means of zinc and hydrochloric acid, in a solution containing arsenic, arsenious hydride is formed, and this, on coming into

* This account of the Arsenic Limit-Test is substantially that given in the Supplementary Report of the Committee of Reference in Pharmacy to the Pharmacopoeia Committee of the General Medical Council, 1912. In actual practice the official process, as here described, is usually considerably modified with the object of ensuring greater speed and accuracy, but the student need only concern himself with the details of the official method.

contact with paper permeated with mercuric chloride, produces a yellow stain, the intensity of which varies according to the quantity of arsenic present. The details of procedure employed in the Pharmacopœia are based upon a paper by C. A. Hill and H. S. Collins (*Chemist and Druggist*, 1905). The amount of arsenic in parts per million is calculated as As_4O_6.

Apparatus Required

A wide-mouthed bottle (A, Fig. 2), capable of holding about 120 mils, and fitted with a rubber bung (C), through which passes a glass tube (D). The latter—made from ordinary soft glass tubing—has a total length of 200 mm. and an internal diameter of 5 mm. (external diameter 7 mm.) and is open at both ends. The upper end is slightly widened to a diameter of 8 mm. while the lower end is drawn out to about 1 mm. diameter and a hole (B) about 2 mm. diameter is blown in the side of the tube where it is constricted.

Lead Papers.—Pieces of thin white filter-paper 100 mm. × 40 mm. soaked in a 10 per cent aqueous solution of lead acetate and dried (F).

Mercuric Chloride Papers.—Circles of smooth white filter-paper 55 mm. diameter soaked in a saturated aqueous solution of mercuric chloride and dried (E). The mercuric chloride papers should be stored in a stoppered bottle in the dark. If exposed to sunlight the mercuric compound becomes reduced and when utilised in an arsenic test affords a lighter-coloured stain.

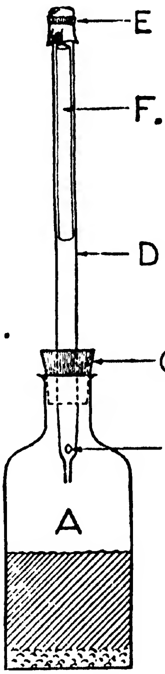


Fig. 2.—Apparatus for Arsenic Test.

Reagents Required

The special reagents for Arsenic Testing are distinguished by the letters "AsT".

Hydrochloric Acid AsT.—This should not contain more than 0·1 part per million of arsenic (As_4O_6) as shown by the Control Test (see under), and should be free from iron.

Sulphuric Acid AsT.—10 grammes tested as described under "Acidum Sulphuricum" (p. 181), but omitting the stannated hydrochloric acid AsT and adding 0·2 mil of stannous chloride solution AsT, should give no visible stain.

Nitric Acid AsT.—10 mils treated as described under "Acidum Nitricum" (p. 181) should give no visible stain.

Stannous Chloride Solution AsT.—Prepared from the B.P.

solution * by adding an equal volume of hydrochloric acid, boiling down to the original bulk and filtering. This should respond to the test for arsenic given below (Control Test).

Bromine Solution AsT—

Bromine	30 grammes.
Potassium bromide	30 grammes.
Water to	100 mils.

This should respond to the test for arsenic given below (Control Test).

Arsenic Solution AsT—

Hydrochloric solution of arsenic, B.P.	1 mil.
Water to	1000 mils.

This solution should be freshly prepared.

1 mil of this diluted solution contains 0·00001 gramme (=one hundredth of one milligramme) As_4O_6.

Zinc AsT (Granulated Zinc).—This should conform to the arsenic requirement involved in the Control Test (see under), and should be free from iron.

Potassium Chlorate AsT.—5 grammes tested as described under "Potassii Chloras" (p. 184), should give no visible stain.

Calcium Hydroxide AsT.—10 grammes tested, as described under "Calcii Hydras" (p. 182), should give no visible stain.

Citric Acid AsT.—10 grammes tested, as described under "Acidum Aceticum" (p. 180), should give no visible stain.

Stannated Hydrochloric Acid AsT (Hydrochloric Acid containing Stannous Chloride):

Stannous chloride solution AsT . .	1 mil.
Hydrochloric acid AsT to . . .	100 mils.

Brominated Hydrochloric Acid AsT (Hydrochloric Acid containing Bromine):

Bromine solution AsT	1 mil.
Hydrochloric Acid AsT to . . .	100 mils.

Method of performing the Quantitative Test for Arsenic

By a variable method of procedure, suitable to the particular needs of each case, there is prepared from the substance to be tested a solution, which may or may not contain the substance to be tested, but in every case contains the whole of the arsenic (if any) originally present in that substance. It is this solution—hereinafter referred to as "the operative solution"—which is introduced into the actual test.

* Solution of Stannous Chloride (Appendix II. *B.P.*) is prepared by adding 20 grammes of granulated tin to a mixture of 60 mils of Hydrochloric Acid and 20 mils of water, and heating gently till gas ceases to be evolved. Sufficient water is then added to produce 100 mils, and the solution is allowed to remain in contact with the undissolved tin.

General Test

A strip of the lead paper is rolled up and placed in the glass tube, so that the upper end is not less than 2 cm. below the top of the tube.

A piece of the mercuric chloride paper is now placed over the top of the tube and secured by means of a rubber ring. The tube is inserted in the rubber bung.

The operative solution of the substance, prepared as specified, is placed in the wide-mouthed bottle and 10 grammes of zinc AsT added. The rubber bung with glass tube attached is quickly placed in position, so that the lower end of the tube is clear above the surface of the liquid and the hole in the constricted portion of the tube is clear below the bottom of the bung. The action should be allowed to proceed for thirty to forty minutes, the mercuric chloride paper not being exposed to strong sunlight. The action may be accelerated by standing the apparatus on a hot plate, care being taken that the mercuric chloride paper remains quite dry throughout the duration of the test.

The yellow stain which is produced on the mercuric chloride paper if arsenic be present is compared, by daylight, with stains produced by operating in a similar manner with known quantities of the arsenic solution AsT.

The comparison of the stains should be made at the completion of the test, and those used for comparison should be freshly prepared. The stains fade upon keeping.

Standard Stain.—Prepare a solution by adding to 50 mils of hot water, 10 mils of stannated hydrochloric acid AsT, and 1 mil of arsenic solution AsT. The resulting solution, when treated as described in the "General Test", will yield a stain on the mercuric chloride paper which will be referred to as the "Standard Stain".

Control Tests for Reagents AsT

Hydrochloric Acid AsT.—To 50 mils of the hydrochloric acid to be tested add 0·2 mil of bromine solution AsT, evaporate on a water-bath until reduced to 16 mils, add 50 mils of hot water and 5 drops of stannous chloride solution AsT, and with this solution carry out the "General Test" described above. The stain produced on the mercuric chloride paper should not be deeper than that given by 10 mils of the same hydrochloric acid with 5 drops of stannous chloride solution AsT, 0·4 mil of arsenic solution AsT, and 50 mils of hot water, showing that the proportion of arsenic present in the hydrochloric acid does not exceed 0·1 part per million.

Stannous Chloride Solution AsT.—To 10 mils of the stannous chloride solution add 6 mils of water and 10 mils of hydrochloric acid AsT, and distil 16 mils. To the distillate add 50 mils of hot water and a few drops of stannous chloride solution AsT, and with this solution carry out the "General Test" described above. The

stain produced on the mercuric chloride paper should not be deeper than the standard stain, showing that the proportion of arsenic present does not exceed 1 part per million.

Bromine Solution AsT.—Evaporate 10 mils of the solution of bromine on a water-bath nearly to dryness, add 50 mils of hot water, 10 mils of hydrochloric acid AsT, and sufficient solution of stannous chloride AsT to reduce the remaining bromine, and with this solution carry out the "General Test" described above. The stain produced on the mercuric chloride paper should not be deeper than the standard stain, showing that the proportion of arsenic present does not exceed 1 part per million.

Zinc AsT.—Add 10 mils of stannated hydrochloric acid AsT to 50 mils of hot water, and with this solution and 10 grammes of zinc AsT proceed as with the "General Test", but allow the action to continue for one hour. No visible stain should be produced on the mercuric chloride paper (limit of arsenic in the zinc).

PREPARATION OF SOLUTION TO BE EXAMINED

The following are the varying methods of preparing the solution to be examined: *The quantities are so arranged that, when tested according to the General Test described above, the stain produced on the mercuric chloride should not be deeper than the Standard Stain, showing that the proportion of arsenic present does not exceed the permissible limit.* (Indicated by the figures in brackets.)

Acidum Aceticum.—5 grammes in 50 mils of hot water, adding 10 mils of stannated hydrochloric acid AsT. (2.)

Acidum Acetylsalicylicum.—5 grammes made into a paste in a porcelain dish with 2 grammes of calcium hydroxide AsT and 5 mils of water, drying and gently igniting, dissolving the residue in 16 mils of brominated hydrochloric acid AsT and 45 mils of hot water, and finally removing excess of bromine by a few drops of solution of stannous chloride AsT. (2.)

Acidum Benzoicum.—5 grammes treated as described under "Acidum Acetylsalicylicum". (2.)

Acidum Boricum.—2 grammes with 4 grammes of citric acid AsT in 50 mils of hot water, adding 10 mils of stannated hydrochloric acid AsT. (5.)

Acidum Citricum.—7 grammes treated as described under "Acidum Aceticum". (1·4.)

Acidum Hydriodicum Dilutum.—2 grammes with 50 mils of hot water, adding 0·5 mil of solution of bromine AsT and 10 mils of hydrochloric acid AsT, allowing it to stand for five minutes, and removing excess of bromine by a few drops of solution of stannous chloride AsT. (5.)

Acidum Hydrobromicum Dilutum.—2 grammes treated as described under "Acidum Aceticum". (5.)

Acidum Hydrochloricum.—2 grammes with 50 mils of hot water and 8 mils of stannated hydrochloric acid AsT. (5.)

Acidum Lacticum.—2 grammes treated as described under "Acidum Aceticum". (5.)

Acidum Nitricum.—2 grammes heated in a porcelain dish with 2 mils of sulphuric acid AsT until white fumes are evolved, then cooling, adding 2 mils of water, again heating until white fumes are evolved, again cooling and adding to the residue 50 mils of hot water and 10 mils of stannated hydrochloric acid AsT. (5.)

Acidum Phosphoricum Concentratum.—2 grammes treated as described under "Acidum Aceticum". (5.)

Acidum Salicylicum.—5 grammes treated as described under "Acidum Acetylsalicylicum". (2.)

Acidum Sulphuricum.—2 grammes mixed with 10 mils of water, adding 40 mils of hot water and 8 mils of stannated hydrochloric acid AsT. (5.)

Acidum Sulphurosum.—2 grammes mixed in the cold with 0·5 gramme of potassium chlorate AsT and 11 mils of hydrochloric acid AsT, warming to expel excess of chlorine, then adding 50 mils of hot water and a few drops of solution of stannous chloride AsT. (5.)

Acidum Tartaricum.—7 grammes treated as described under "Acidum Aceticum". (1·4.)

Alumen Purificatum.—2 grammes treated as described under "Acidum Aceticum". (5.)

Ammonii Benzoas.—5 grammes treated as described under "Acidum Acetylsalicylicum". (2.)

Ammonii Bromidum.—2 grammes in 50 mils of hot water, adding 12 mils of stannated hydrochloric acid AsT. (5.)

Ammonii Carbonas.—5 grammes in 50 mils of hot water, boiled gently until the greater part of the ammonium carbonate is volatilised, then adding 15 mils of brominated hydrochloric acid AsT and removing excess of the bromine by a few drops of solution of stannous chloride AsT. (2.)

Ammonii Chloridum.—2 grammes treated as described under "Acidum Aceticum". (5.)

Antimonium Sulphuratum.—0·01 gramme dissolved by boiling in a small flask with 0·2 gramme of calcium hydroxide AsT and 5 mils of water, then adding 2 mils of solution of bromine AsT and again gently boiling, then adding 17 mils of hydrochloric acid AsT and 5 mils of water, and boiling until most of the bromine is volatilised, the last traces being removed by adding a slight excess of solution of stannous chloride AsT, connecting to a condenser, and distilling 20 mils, then washing the condenser and flask, returning the distillate to the flask, adding 1 drop of solution of stannous chloride AsT, and redistilling 16 mils, then adding to the distillate 45 mils of hot water and a few drops of solution of stannous chloride AsT. (1000.)

Bismuthi Carbonas.—5 grammes dissolved in a small flask in 5 mils of water and 20 mils of brominated hydrochloric acid AsT, removing excess of bromine by a few drops of solution of stannous chloride AsT, connecting to a condenser and distilling 18 mils, then

adding to the distillate 40 mils of hot water and 3 drops of solution of stannous chloride AsT. (2.)

Bismuthi Salicylas.—5 grammes made into a paste in a porcelain dish with 1 gramme of calcium hydroxide AsT and 5 mils of water, drying and gently igniting, dissolving the residue in 20 mils of brominated hydrochloric acid AsT and 10 mils of water, transferring to a small flask, and adding sufficient solution of stannous chloride AsT to remove the excess of bromine, connecting to a condenser, and distilling 20 mils, then adding to the distillate 40 mils of hot water and 3 drops of solution of stannous chloride AsT. (2.)

Bismuthi Subnitras.—5 grammes heated in a porcelain dish with 2 mils of sulphuric acid AsT until white fumes are evolved, cooling, adding 5 mils of water and again heating until white fumes are evolved, dissolving the residue when cold in 20 mils of water and 10 mils of stannated hydrochloric acid AsT, transferring to a small flask, connecting to a condenser and distilling 20 mils, adding to the distillate a little solution of bromine AsT to oxidise any sulphurous acid, removing excess of bromine by a few drops of solution of stannous chloride AsT, and adding 40 mils of hot water. (2.)

Borax Purificatus.—2 grammes with 4 grammes of citric acid AsT in 50 mils of hot water, adding 12 mils of stannated hydrochloric acid AsT. (5.)

Calcii Carbonas Præcipitatus.—2 grammes in 14 mils of brominated hydrochloric acid AsT and 45 mils of hot water, removing excess of bromine by a few drops of solution of stannous chloride AsT.

Calcii Chloridum.—2 grammes treated as described under "Acidum Aceticum". (5.)

Calcii Hydras.—2 grammes in 16 mils of brominated hydrochloric acid AsT, and 45 mils of hot water, removing excess of bromine by a few drops of solution of stannous chloride AsT. (5.)

Calcii Hypophosphis.—2 grammes mixed in the cold with 2 grammes of potassium chlorate and 18 mils of hydrochloric acid AsT, then warming to expel excess of chlorine, adding 40 mils of hot water and a few drops of solution of stannous chloride AsT. (5.)

Calcii Lactas.—2 grammes treated as described under "Ammonii Bromidum". (5.)

Calcii Phosphas.—2 grammes in 50 mils of hot water and 14 mils of stannated hydrochloric acid AsT. (5.)

Calx.—2 grammes in 18 mils of brominated hydrochloric acid AsT and 40 mils of water, removing excess of bromine by a few drops of solution of stannous chloride AsT. (5.)

Creta Præparata.—2 grammes treated as described under "Calcii Carbonas Præcipitatus". (5.)

Cupri Sulphas.—1 gramme dissolved in a small flask with 10 mils of water and 15 mils of hydrochloric acid AsT, adding 5 drops of solution of stannous chloride AsT, connecting to a condenser, and distilling 20 mils, adding a little solution of bromine to the

distillate to oxidise any sulphurous acid, removing excess of bromine by a few drops of solution of stannous chloride AsT, finally adding 40 mils of hot water. (10.)

Ferri Carbonas Saccharatus.—2 grammes made into a paste with 1 gramme of calcium hydroxide AsT and 2 mils of water in a porcelain dish, drying and gently igniting, dissolving the residue in 20 mils of brominated hydrochloric acid AsT and 10 mils of water, transferring to a small flask, adding solution of stannous chloride AsT until the yellow colour disappears, then connecting to a condenser and distilling 24 mils, finally adding to the distillate 35 mils of hot water and 3 drops of solution of stannous chloride AsT. (5.)

Ferri et Ammonii Citras.—2 grammes treated as described under "Ferri Carbonas Saccharatus". (5.)

Ferri et Potassii Tartras.—2 grammes treated as described under "Ferri Carbonas Saccharatus". (5.)

Ferri et Quininæ Citras.—2 grammes treated as described under "Ferri Carbonas Saccharatus". (5.)

Ferri Phosphas Saccharatus.—2 grammes treated as described under "Ferri Carbonas Saccharatus". (5.)

Ferri Sulphas.—5 grammes dissolved in a small flask with 10 mils of water and 15 mils of hydrochloric acid AsT, adding solution of stannous chloride AsT until the yellow colour disappears, connecting to a condenser and distilling 20 mils, adding a little solution of bromine AsT to the distillate to oxidise any sulphurous acid, removing excess of bromine by a few drops of solution of stannous chloride AsT, and finally adding 40 mils of hot water. (2.)

Ferri Sulphas Exsiccatus.—2 grammes treated as described under "Ferri Sulphas". (5.)

Ferrum.—0·05 gramme mixed in a small flask with 0·1 gramme of potassium chlorate AsT and 7 mils of water, adding 11 mils of hydrochloric acid AsT and, when the reaction has ceased and all the iron is dissolved, boiling gently to expel chlorine, then adding solution of stannous chloride AsT until the yellow colour disappears, connecting to a condenser and distilling 14 mils, finally adding to the distillate 50 mils of hot water and a few drops of solution of stannous chloride AsT. (200.)

Ferrum Redactum.—0·05 gramme treated as described under "Ferrum". (200.)

Glucosum.—5 grammes treated as described under "Acidum Hydriodicum Dilutum". (2.)

Glycerinum.—2·5 grammes treated as described under "Acidum Aceticum". (4.)

Liquor Ammoniæ Fortis.—20 grammes evaporated on a water-bath until reduced to 5 mils, adding 40 mils of water, and 15 mils of brominated hydrochloric acid AsT, and removing excess of bromine by a few drops of solution of stannous chlorine AsT. (0·5.)

Liquor Ferri Perchloridi Fortis.—1 gramme heated in a porcelain dish with 1 mil of sulphuric acid AsT until white fumes are evolved, cooling, adding an equal volume of water, and again heating until

white fumes are evolved, dissolving the residue in 10 mils of water and 15 mils of hydrochloric acid AsT, transferring to a small flask, adding solution of stannous chloride AsT until the yellow colour disappears, connecting to a condenser and distilling 20 mils, adding to the distillate a little solution of bromine AsT to oxidise any sulphurous acid, removing excess of bromine by a few drops of solution of stannous chloride AsT, and then adding 40 mils of hot water. (10.)

Liquor Ferri Persulphatis.—2 grammes treated as described under "Liquor Ferri Perchloridi Fortis". (5.)

Liquor Magnesii Bicarbonatis.—50 mils with 13 mils of brominated hydrochloric acid AsT, removing excess of bromine by a few drops of solution of stannous chloride AsT. (0·2.)

Lithii Carbonas.—2 grammes treated as described under "Calcii Hydras". (5.)

Lithii Citras.—5 grammes in 45 mils of hot water, adding 15 mils of stannated hydrochloric acid AsT. (2.)

Magnesia Levis.—2 grammes with 40 mils of water and 20 mils of brominated hydrochloric acid AsT, removing excess of bromine by a few drops of solution of stannous chloride AsT. (5.)

Magnesia Ponderosa.—2 grammes treated as described under "Magnesia Levis". (5.)

Magnesii Carbonas Levis.—2 grammes in 45 mils of hot water and 15 mils of brominated hydrochloric acid AsT, removing excess of bromine by a few drops of solution of stannous chloride AsT. (5.)

Magnesii Carbonas Ponderosus.—2 grammes treated as described under "Magnesii Carbonas Levis". (5.)

Magnesii Sulphas.—2 grammes treated as described under "Acidum Aceticum". (5.)

Potassii Acetas.—2 grammes treated as described under "Ammonii Bromidum". (5.)

Potassii Bicarbonas.—2 grammes in 50 mils of hot water, adding 12 mils of brominated hydrochloric acid AsT, removing excess of bromine by a few drops of solution of stannous chloride AsT. (5.)

Potassii Bromidum.—2 grammes treated as described under "Ammonii Bromidum". (5.)

Potassii Carbonas.—5 grammes in 50 mils of hot water, adding 16 mils of brominated hydrochloric acid AsT, removing excess of bromine by a few drops of solution of stannous chloride AsT. (2.)

Potassii Chloras.—2 grammes mixed in the cold with 10 mils of water and 20 mils of hydrochloric acid AsT, and, when the reaction is complete, warming to expel chlorine, then adding a few drops of solution of stannous chloride AsT and 30 mils of hot water. (5.)

Potassii Citras.—5 grammes treated as described under "Lithii Citras". (2.)

Potassii Iodidum.—2 grammes treated as described under "Ammonii Bromidum". (5.)

Potassii Nitras.—2 grammes heated in a porcelain dish with 2 mils of sulphuric acid AsT and 5 mils of water until white fumes are evolved, cooling, adding 3 mils of water and again heating until white fumes are evolved, finally cooling and adding to the residue 50 mils of hot water and 10 mils of stannated hydrochloric acid AsT. (5.)

Potassii Sulphas.—2 grammes treated as described under "Acidum Aceticum". (5.)

Potassii Tartras.—5 grammes treated as described under "Calcii Phosphas". (2.)

Potassii Tartras Acidus.—5 grammes in 50 mils of hot water and 13 mils of brominated hydrochloric acid AsT, removing excess of bromine by a few drops of solution of stannous chloride AsT. (2.)

Sodii Benzoas.—5 grammes gently heated in a porcelain dish, until inflammable vapours cease to be evolved, dissolving the residue (ignoring any carbon) in 14 mils of brominated hydrochloric acid AsT and 50 mils of hot water and removing excess of bromine by a few drops of solution of stannous chloride AsT. (2.)

Sodii Bicarbonas.—5 grammes treated as described under "Potassii Carbonas". (2.)

Sodii Bromidum.—2 grammes treated as described under "Ammonii Bromidum". (5.)

Sodii Carbonas.—5 grammes in 50 mils of hot water, adding 14 mils of brominated hydrochloric acid AsT and removing excess of bromine by a few drops of solution of stannous chloride AsT. (2.)

Sodii Carbonas Exsiccatus.—2 grammes treated as described under "Sodii Carbonas". (5.)

Sodii Chloridum.—5 grammes treated as described under "Acidum Aceticum". (2.)

Sodii et Potassii Tartras.—5 grammes treated as described under "Calcii Phosphas". (2.)

Sodii Hypophosphis.—2 grammes treated as described under "Calcii Hypophosphis". (5.)

Sodii Iodidum.—2 grammes in 50 mils of hot water, adding 11 mils of stannated hydrochloric acid AsT. (5.)

Sodii Nitris.—2 grammes treated as described under "Potassii Nitras". (5.)

Sodii Phosphas.—2 grammes treated as described under "Acidum Aceticum". (5.)

Sodii Phosphas Acidus.—5 grammes treated as described under "Acidum Aceticum". (2.)

Sodii Salicylas.—5 grammes treated as described under "Sodii Benzoas". (2.)

Sodii Sulphas.—5 grammes treated as described under "Acidum Aceticum". (2.)

Sodii Sulphis.—2 grammes with 0·5 gramme of potassium chlorate AsT in 5 mils of warm water, adding 12 mils of hydrochloric acid AsT, then warming to expel excess of chlorine and

adding 45 mils of hot water and a few drops of solution of stannous chloride AsT. (5.)

Strontii Bromidum.—2 grammes treated as described under "Ammonii Bromidum". (5.)

Sulphur Præcipitatum.—2 grammes digested for one hour on a water-bath with 50 mils of water and 5 mils of Solution of Ammonia, filtering and evaporating the filtrate to low bulk, adding 10 mils of nitric acid AsT and boiling to oxidise any sulphur, then adding 2 mils of sulphuric acid AsT and heating until white fumes are evolved, cooling, adding 2 mils of water and again heating until white fumes are evolved, finally adding 50 mils of hot water and 10 mils of stannated hydrochloric acid AsT. (5.)

Sulphur Sublimatum.—2 grammes treated as described under "Sulphur Præcipitatum". (5.)

Zinci Acetas.—2 grammes treated as described under "Ammonii Bromidum". (5.)

Zinci Carbonas.—1 gramme treated as described under "Potassii Carbonas". (10.)

Zinci Chloridum.—2 grammes treated as described under "Acidum Aceticum". (5.)

Zinci Oxidum.—1 gramme treated as described under "Potassii Carbonas". (10.)

Zinci Sulphas.—2 grammes treated as described under "Acidum Aceticum". (5.)

Zinci Valerianas.—2 grammes made into a paste in a porcelain dish with 2 grammes of calcium hydroxide AsT and 5 mils of water, drying and gently igniting, then dissolving the residue in 18 mils of brominated hydrochloric acid AsT and 40 mils of hot water and removing excess of bromine by a few drops of solution of stannous chloride AsT. (5.)

PART II

ORGANIC

CHAPTER XIII

THE ELEMENTS PRESENT IN ORGANIC COMPOUNDS

Many chemical compounds have been known from very early times which are produced in Nature as a result of the vital processes of plants or animals. Among the more important of these may be mentioned sugars, starches, alkaloids, glucosides, and essential oils of plants.

The division of chemistry into its two main branches appears to have been first proposed by Nicolas Lemery in his *Cours de Chimie* (1675), in which substances which are produced by animal or vegetable organisms were classed as *organic* compounds, in contradistinction to mineral or *inorganic* compounds, such as salt, nitre, or oil of vitriol. It was long thought that there was a fundamental difference between the two classes; the early chemists believed that organic compounds were produced through the agency of some "vital force", and that it would therefore be impossible to prepare any organic compound artificially in the laboratory. This view persisted until well into the nineteenth century, but was gradually abandoned after the discovery that organic compounds obeyed the ordinary laws of chemical combination, and that many of them could be built up from their elements, in the laboratory, without the aid of any vital force.

More than a century ago, the French chemist Lavoisier discovered that nearly all animal and vegetable products contain the element carbon, and the term *organic*, though bereft of its original meaning, is still used to distinguish the carbon compounds from the compounds of other elements. This classification is retained for two reasons. First, the known compounds of carbon are far more numerous than those of any other element; second, they have certain characteristics in common which are not shared by the compounds of the other elements. It should be clearly understood that the present distinction between organic and inorganic chemistry is simply one of convenience, and that it is not always rigidly adhered to in practice. For example, carbon monoxide and carbon dioxide, though, strictly speaking, organic compounds, are usually dealt with in text-books of inorganic chemistry, on account of their wide distribution and general interest.

The Composition of Organic Compounds.—Most organic compounds, including nearly all vegetable products, contain the elements

carbon, hydrogen, and oxygen; many animal and some vegetable substances contain in addition nitrogen. Other elements, such as sulphur, phosphorus, and the halogens, are sometimes met with in organic compounds, and the metallic salts of organic acids may contain any metal.

Detection of the Elements in an Organic Compound

Carbon can often be detected in a substance by heating it strongly on a crucible lid or a piece of platinum foil, when the substance may char, giving a black carbonaceous mass which slowly burns away on prolonged heating. Many carbon compounds char when heated with concentrated sulphuric acid, yielding a dark-coloured solution in which black particles can be seen. At the same time some of the sulphuric acid is usually reduced to sulphur dioxide, and oxides of carbon may be evolved.

A more certain way of detecting the presence of carbon consists in strongly heating the substance, mixed with powdered copper oxide, in a hard glass tube. Under these conditions the carbon is oxidised to carbon dioxide, which may be detected by passing the evolved gases through lime-water.

Hydrogen may be detected by the formation of drops of water on the cool portions of the tube during the last-mentioned test.

Nitrogen can be detected in an organic substance in the following way. About 0·2 gramme of the substance is placed in a small dry test tube or ignition tube, together with a piece of metallic sodium no larger than a pea. The tube is heated, very gently at first and finally to redness until all action ceases. The heated portion of the tube is then plunged into about 10 mils of water contained in an evaporating dish. The water is heated to boiling, and filtered to remove carbonaceous matter and fragments of glass. To the filtrate a few drops of ferrous sulphate and ferric chloride solutions are added, and, after boiling, the liquid is acidified with dilute hydrochloric acid. The presence of nitrogen is shown by the formation of a blue precipitate or a greenish-blue colour.

In this test the sodium combines with some of the carbon and nitrogen present to form sodium cyanide, which, on boiling with ferrous hydroxide (formed by the addition of ferrous sulphate to the alkaline solution), is converted into sodium ferrocyanide, $6NaCN + Fe(OH)_2 = Na_4Fe(CN)_6 + 2NaOH$, and this, on acidification, reacts with the ferric salt present to form "Prussian blue".

Halogens can often be detected by heating the substance in a bunsen flame on a piece of clean copper wire, when, owing to the formation of the volatile chloride, bromide, or iodide of copper, the flame is coloured green. The colour is not given by all organic halogen compounds, and in some cases a green flame may be formed when no halogen is present. The following method is much more reliable. The substance is heated with sodium and the product extracted with water as described in the test for nitrogen.

The aqueous extract is then acidified with nitric acid, and, if nitrogen be present, is boiled until all the hydrocyanic acid is expelled. Silver nitrate solution is then added, when a precipitate of silver chloride, bromide, or iodide proves the presence in the original substance of the corresponding halogen.

Sulphur and phosphorus can be tested for by fusing the substance with a mixture of potassium carbonate and nitrate, when any sulphur or phosphorus is oxidised to potassium sulphate or potassium phosphate respectively. It is only necessary, therefore, to extract the melt with water and apply to the solution the usual tests for sulphate and phosphate.

Metals.—It is often necessary to test for metals in an organic salt. The salt is heated to redness on a crucible lid or a piece of platinum foil, when, if any residue remains after all the carbon has burned away, a metal is present, and this can be identified in the residue by the ordinary methods of qualitative analysis. It should be noted, however, that compounds of arsenic or mercury will volatilise completely during this test, leaving no residue.

Quantitative Estimation of the Elements

Estimation of Carbon and Hydrogen.—The carbon and hydrogen in an organic substance may be quantitatively estimated by burning the substance in a stream of oxygen and leading the products of combustion over red-hot copper oxide in order to ensure complete oxidation. The hydrogen is completely converted into water, which can be collected in a tube containing anhydrous calcium chloride, whilst the carbon is converted into carbon dioxide, which can be absorbed in a solution of potassium hydroxide.

The combustion is effected in a hard glass tube about thirty inches long and three-quarters of an inch in diameter, Fig. 3. About one-half to two-thirds of the length of the tube (CB) is filled with granulated copper oxide. The tube is then placed in a "combustion furnace", and the part containing the copper oxide is heated to redness by lighting those burners of the furnace directly beneath it, a slow stream of dry air being passed at the same time through the tube in the direction AB. This is done with the object of

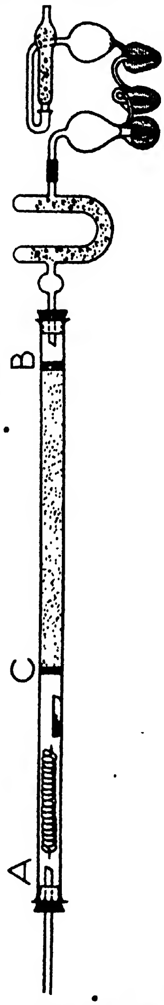


FIG. 3.—Estimation of carbon and hydrogen.

driving off all traces of moisture from the copper oxide. When the tube is quite dry, a U-tube containing anhydrous calcium chloride, previously carefully weighed, is attached to the end, B, of the combustion tube by means of a rubber bung, and a set of "potash bulbs", containing a strong solution of potassium hydroxide, also previously weighed, is attached to the calcium chloride tube by a short piece of rubber tubing. About 0·2 gramme of the substance to be analysed is weighed out in a small porcelain "boat", and the boat is pushed into the combustion tube from the end A; behind it is introduced a roll of dry oxidised copper gauze, to prevent any backward diffusion of the products of combustion. A slow current of dry oxygen is now admitted at the end A, and the combustion is started by lighting the remaining burners of the furnace, commencing at A. When the whole tube has been raised to a red heat, and the substance has completely burned away, the oxygen is turned off, and a slow stream of air is passed through to sweep all the carbon dioxide into the potash bulbs. The furnace is then allowed to cool, and the potash bulbs and calcium chloride tube are disconnected and separately weighed.

The increase in weight of the calcium chloride tube gives the weight of water formed, whilst the increase in weight of the potash bulbs gives the weight of carbon dioxide produced, and, from these results, the percentages of hydrogen and of carbon in the substance analysed can be calculated. If the substance contains only carbon, hydrogen, and oxygen, the percentage of oxygen can be calculated by difference.

Example: 0·2461 gramme of a substance gave 0·7037 gramme of carbon dioxide and 0·1209 gramme of water.

The ratio $C : CO_2 :: 3 : 11$.
The ratio $H : H_2O :: 1 : 9$.

$$\text{Hence percentage of carbon} = \frac{0{\cdot}7037 \times 3 \times 100}{0{\cdot}2461 \times 11} = 77{\cdot}98.$$

$$\text{Percentage of hydrogen} = \frac{0{\cdot}1209 \times 100}{0{\cdot}2461 \times 9} = 5{\cdot}46.$$

Percentage of oxygen by difference $= 100 - 83{\cdot}44 = 16{\cdot}$[illegible]

Estimation of Nitrogen.—There are three methods in common use for the estimation of nitrogen in organic compounds.

Dumas' Method.—The substance is heated with copper oxide in an atmosphere of carbon dioxide, when it is completely decomposed into carbon dioxide, water, and nitrogen. The nitrogen is collected over strong potassium hydroxide solution and measured. The carbon dioxide is, of course, dissolved by the potash.

The analysis is carried out in a combustion tube, the greater part of which is filled with an intimate mixture of copper oxide and a weighed amount of the substance under examination. At one end of the tube is inserted a roll of bright copper gauze, the object of which is to decompose any oxides of nitrogen formed during the

combustion. A stream of carbon dioxide is passed through the tube from the end farthest from the copper gauze for about half an hour, in order to expel all the air, and, during this time, the portion of the tube containing the copper gauze is heated to redness. The combustion is then started by gradually heating the rest of the tube to redness, and the evolved nitrogen is collected in a eudiometer tube over strong potassium hydroxide solution. When the combustion is finished, more carbon dioxide is passed, in order to sweep the last traces of nitrogen into the eudiometer. The weight of nitrogen can be calculated from the measured volume, and from this weight the percentage of nitrogen in the substance can be calculated. It is, of course, necessary to correct the volume of nitrogen for temperature and pressure, and for the tension of aqueous vapour.

Example: 0·1037 gramme of a substance gave 13·2 mils of moist nitrogen at 10° and 759 m.m.

Tension of aqueous vapour at 10° is 9·14 m.m.;

$\therefore$ Volume of nitrogen at N.T.P. $= \dfrac{13{\cdot}2 \times 750 \times 273}{760 \times 283} = 12{\cdot}57$ mils.

Since 1 mil of nitrogen at N.T.P. weighs 0·001251 gramme, the weight of the nitrogen is

$$12{\cdot}57 \times {\cdot}001251 = {\cdot}01573 \text{ gramme};$$

$\therefore$ Percentage of nitrogen in the substance

$$= \frac{{\cdot}01573}{0{\cdot}1037} \times 100 = 15{\cdot}17.$$

The Soda-lime or *Will and Varrentrap's Method* depends on the fact that the nitrogen in most organic compounds is completely converted into ammonia by heating the substance with solid soda-lime.

A piece of combustion tubing about 15 inches long is bent at one end at an angle and drawn out to a point. Into the tube are

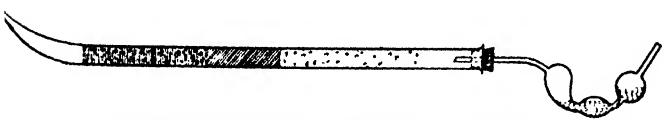


FIG. 4.—Estimation of Nitrogen (Soda-lime Method).

introduced, first, some coarsely powdered soda-lime, then an intimate mixture of soda-lime with a weighed amount of the substance, and finally, some more pure soda-lime. The open end of the tube is then connected to a set of specially designed absorption bulbs containing a known volume of standard hydrochloric acid. The tube is raised to a red heat, starting with the end nearest the absorption bulbs. When ammonia ceases to be evolved the tip of the closed end of the combustion tube is broken off, and a current of air is

drawn through the apparatus in order to sweep into the bulbs the small quantity of ammonia remaining in the combustion tube.

The partially neutralised acid is then transferred from the bulbs to a flask, and titrated with standard sodium hydroxide solution. In this way the amount of ammonia absorbed is determined, and the percentage of nitrogen can be calculated.

Example : 0·5346 gramme of a substance was employed.

The evolved ammonia was collected in 25 mils of N/2 hydrochloric acid. To neutralise the excess of acid 14·2 mils of N/2 sodium hydroxide was required.

Hence the evolved ammonia was equivalent to 25 − 14·2 = 10·8 mils of N/2 acid;

$$\therefore \text{ Weight of ammonia} = \frac{10{\cdot}8 \times 0{\cdot}017}{2} = 0{\cdot}0918 \text{ gramme.}$$

$$\text{This is equivalent to } \frac{0{\cdot}0918 \times 14}{17} \text{ gramme of nitrogen;}$$

∴ Percentage of nitrogen in substance

$$= \frac{0{\cdot}0918 \times 14 \times 100}{17 \times 0{\cdot}5346} = 14{\cdot}14.$$

The Kjeldahl Method.—A weighed amount of the substance (about 0·5 gramme is usually employed) is heated with about 10 mils of concentrated sulphuric acid in a round-bottomed flask. At first the acid becomes dark in colour, owing to the separation of carbonaceous matter, but the heating is continued until the liquid is almost colourless. In this way the nitrogen in the substance is converted into ammonium sulphate. The liquid is diluted, mixed with strong sodium hydroxide solution, and the liberated ammonia is distilled into a measured volume of standard acid, the excess of acid being then estimated by titration with standard alkali. The calculation is exactly similar to that of the soda-lime method.

The Kjeldahl method is very convenient, and can be quickly and accurately carried out. It is widely employed for the analysis of commercial nitrogenous products. The disadvantage of both the Kjeldahl and the soda-lime methods is that they are not universally applicable. Many organic nitrogenous compounds are known which do not yield ammonia when heated with soda-lime, and which are not decomposed by sulphuric acid with formation of ammonium sulphate. In such cases the method of Dumas must be employed.

Estimation of Halogens.—Halogens can be estimated quantitatively in organic substances by the method of Carius. A weighed amount of the substance is introduced into a tube of stout glass about 15 inches long and three-quarters of an inch in diameter, sealed at one end. About 10 mils of fuming nitric acid and a little solid silver nitrate are added, and the open end of the tube is then sealed off. The sealed tube is heated in a furnace at 150-200° for an hour or two, during which time the halogen in the organic substance is completely converted into silver chloride, bromide, or

iodide, as the case may be. When cold, the tube is broken, using special precautions owing to the pressure of the gases in the tube, the contents are poured into water, and the insoluble silver halide is filtered off and weighed.

Example: 0·1834 gramme of a substance gave 0·1026 gramme of silver chloride. Since 143·5 grammes of silver chloride contain 35·5 grammes of chlorine, the percentage of chlorine in the substance will be

$$\frac{0{\cdot}1026 \times 35{\cdot}5 \times 100}{0{\cdot}1834 \times 143{\cdot}5} = 13{\cdot}84.$$

Sulphur and **phosphorus** can be estimated by a method based on the way already given for their qualitative detection (p. 191).

CHAPTER XIV

EMPIRICAL, MOLECULAR, AND CONSTITUTIONAL FORMULÆ

The empirical formula of a compound is the simplest possible formula as calculated from a quantitative analysis, and shows only the relative numbers of the various atoms composing the compound. The empirical formula can be calculated from the results of a quantitative analysis by dividing the percentage of each element by its atomic weight, and expressing the ratio in the simplest possible whole numbers. An example will make this clear.

Example : The percentage composition of a compound, as determined by a combustion, is as follows :

$$C = 39{\cdot}86,$$
$$H = 6{\cdot}68;$$
$$O = 53{\cdot}46 \text{ (by difference).}$$

Calculate its empirical formula.

Since an atom of carbon is twelve times as heavy, and an atom of oxygen sixteen times as heavy, as an atom of hydrogen, we must, in order to obtain the ratio of the numbers of the different atoms, divide the percentage of carbon by 12, and the percentage of oxygen by 16. Thus

$$C = \frac{39{\cdot}86}{12} = 3{\cdot}32,$$

$$H = \frac{6{\cdot}68}{1} = 6{\cdot}68,$$

$$O = \frac{53{\cdot}46}{16} = 3{\cdot}34.$$

Expressing these results in the smallest possible whole numbers (and allowing for experimental error) we find that the ratio of C : H : O is as 1 : 2 : 1, so that the empirical formula of the compound is CH_2O.

The molecular formula of a compound shows, not only the ratio of the atoms, but also the *actual numbers* of the various atoms in each molecule, and must be either identical with, or some multiple of, the empirical formula. To make this clear, the empirical and molecular formulæ of a few well-known compounds are given below :

Compound.	Empirical formula.	Molecular formula.
Water	H_2O	H_2O
Hydrogen chloride . .	HCl	HCl
Hydrogen peroxide . .	HO	H_2O_2
Acetic acid . . .	CH_2O	$C_2H_4O_2$
Glucose	CH_2O	$C_6H_{12}O_6$

If the empirical formula of a compound is known as a result of an accurate quantitative analysis, and if by some means the molecular weight of the compound can be determined, then the molecular formula can be easily calculated.

Example : The molecular weight of a compound is 90. Its empirical formula is known to be CH_2O. If this were also its molecular formula, its molecular weight would be $(12+2+16)=30$; but this is one-third of the actual molecular weight, so that the molecular formula of the compound must be $C_3H_6O_3$.

It will therefore be seen that methods for the determination of the molecular weights of compounds are of the greatest importance. Three such methods will now be briefly described.

Victor Meyer's Vapour Density Method.—From Avogadro's theory we know that the density of any gas or vapour (corrected to N.T.P.) is equal to half its molecular weight. So that, if we can determine the vapour density of a compound, it is only necessary to multiply by two in order to obtain its molecular weight. In the case of a gas, the density can be determined by direct weighing. Victor Meyer's method is a way of determining the vapour density of volatile liquids. The apparatus (Fig. 5) consists of a bulb tube (A) about 24 inches long, which is closed at the top by means of a stopper, and is provided with a side tube dipping under water contained in a trough. The outer jacket (B) contains some high boiling-point liquid, such as amyl alcohol, and by boiling this briskly the tube (A) is raised to a constant high temperature. When the temperature becomes steady, as indicated by the fact that bubbles of air cease to be expelled through the water, a graduated tube (C), filled with water, is inverted over the end of the side tube as shown. The stopper is now withdrawn, and a weighed amount of the liquid, contained in a small glass bottle, is dropped into the tube (A), the stopper being quickly replaced.[1] The liquid immediately vaporises, and the vapour drives out a corresponding volume of air into the tube (C). From this volume of air the vapour density of the liquid is calculated.

[1] Before commencing the experiment a piece of cotton-wool is placed at the bottom of the tube (A) in order to prevent fracture when the bottle is dropped in.

Since the volume of the expelled air is measured in C at atmospheric temperature, this volume is equal to the volume which the vapour of the liquid employed would occupy at atmospheric temperature and pressure. It is not necessary, therefore, to know the temperature of the tube (A), but it is very important that this temperature should be steady and sufficiently high to cause rapid

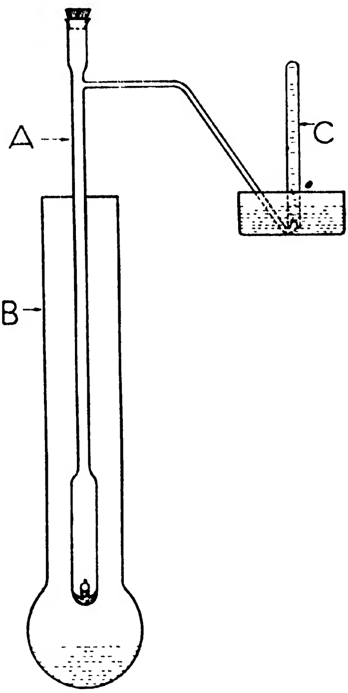


FIG. 5.—Victor Meyer's Vapour Density Apparatus.

vaporisation of the liquid. (As a rule, it is necessary to have the temperature of A at least 20° higher than the boiling-point of the liquid whose vapour density is being determined.)

Example : 0·0837 gramme of a liquid gave 28·7 mils of air, measured at 12° and 752 m.m. pressure. The tension of aqueous vapour at 12° is 10·4 m.m.

$$\text{Volume of air corrected to N.T.P.} = \frac{28 \cdot 7 \times 273 \times 742}{285 \times 760} = 26 \cdot 8 \text{ mils.}$$

Now 26·8 mils of hydrogen at N.T.P. would weigh

$$\frac{0\cdot09 \times 26\cdot8}{1000} = 0\cdot00241 \text{ gramme};$$

∴ Vapour density of liquid

$$= \frac{\text{Weight of vapour}}{\text{Weight of equal volume of hydrogen}} = \frac{0\cdot0837}{0\cdot00241} = 34\cdot7;$$

∴ Molecular weight of liquid $= 34\cdot7 \times 2 = 69\cdot4$.

Vapour densities determined by Victor Meyer's method are not, as a rule, very accurate. This is usually of no importance, as the experimentally determined molecular weight is only used to decide what multiple of the empirical formula shall represent the molecular formula.

Raoult's or *The Cryoscopic Method.*—This method for determining molecular weights does not depend on vapour density measurements, and is, consequently, applicable to non-volatile solids. The freezing-point of a solution is always lower than that of the pure solvent, and it has been found that, for fairly dilute solutions, the amount of depression of the freezing-point is, in general, independent of the nature of the dissolved substance, but is directly proportional to the number of molecules of the substance in a definite quantity of a particular solvent. From this it follows that, if we take equal weights (say 1 gramme) of various substances and dissolve them in equal quantities of a particular liquid, then the depression of the freezing-point in each case will be inversely proportional to the molecular weight of the dissolved substance. This is the principle of the cryoscopic method for the determination of molecular weights. The actual relationship between the depression of the freezing-point and the molecular weight of a dissolved substance is given by the equation

$$M = \frac{K \times C}{D},$$

where M = the required molecular weight, C = concentration of dissolved substance in grammes per 100 grammes of solvent, D = observed depression of the freezing-point, and K is a constant which depends on the nature of the solvent employed. For any particular solvent, K can be determined by observing the depression in the case of some dissolved substance of known molecular weight. Any liquid for which the constant K has been found can be used to determine molecular weights. The calculation is simple.

Example **: 0·2478 gramme of a substance dissolved in 12·99 grammes of benzene lowered the freezing-point by 0·540°. K for benzene is 50. Find the molecular weight of the substance.**

The concentration of the substance is

$$\frac{0.2478 \times 100}{12.99} = 1.907 \text{ grammes per 100 grammes}$$

of benzene.

Then $$M = \frac{K \times C}{D} = \frac{50 \times 1.907}{0.54} = 176.5.$$

The method only gives accurate results when dilute solutions are employed, and consequently the depressions obtained in practice are very small, as can be seen in the above example. The freezing-point of both the pure solvent and the solution are determined in a special apparatus by the aid of a Beckmann thermometer, which can be read to $\frac{1}{500}$ of a degree. The apparatus consists of a boiling-tube containing the liquid or solution, with the bulb of the thermometer immersed in it. Cooling down to the freezing-point is effected by means of a freezing mixture contained in an outer vessel. It should be noted that it is unnecessary to know the actual freezing-point of solvent or solution so long as the *difference* is accurately measured.

The Ebullioscopic Method.—Corresponding to the depression of the freezing-point, dissolved substances cause an elevation of the boiling-point of a liquid. From the extent of this elevation the molecular weight of the dissolved substance can be calculated by means of a formula similar to that already given for the lowering of the freezing-point. The boiling-point or ebullioscopic method presents many experimental difficulties, and does not, as a rule, give such accurate results as does the cryoscopic method.

Constitutional Formulæ.—The study of organic chemistry is much simplified by the use of what are known as "structural" or "constitutional" formulæ, which show, not only the number and kind of the various atoms, but also their arrangement within the molecule.

For the purpose of writing structural formulæ, the valency of an element is represented by attaching the necessary number of lines to the symbol representing an atom of the element. For example, hydrogen and chlorine being univalent are represented by

H— and Cl—,

oxygen and sulphur being bivalent by

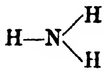
—O— or O= and —S— or S=,

and carbon being quadrivalent by

$$-\overset{|}{\underset{|}{C}}- \text{ or } C\equiv.$$

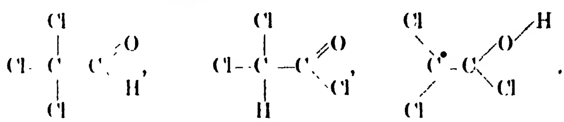
In a constitutional formula the atoms composing the molecule are represented as being linked together by these lines or "valency

bonds ". Thus the formulæ for water, carbon dioxide, and ammonia may be represented

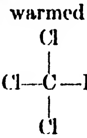
H—O—H, O=C=O, and  respectively.

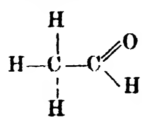
Such formulæ are designed to give some idea of the way in which the molecules are built up. Thus in carbon dioxide the two oxygen atoms are supposed to be joined each to the carbon atom, and not directly to each other. The valency of each atom in the molecule must be correctly shown by the number of bonds attached to that atom ; the length and direction of the bonds is quite immaterial.

In the examples given so far, the structural formulæ have been written from considerations of valency alone. In the case of more complex molecules this cannot generally be done. The compound chloral, for example, has the molecular formula C_2HCl_3O. Now, assuming that all the atoms exert their normal valencies, a number of possible formulæ suggest themselves for this compound, such as :



(1) (2) (3)

In order to decide which of these formulæ correctly represents the arrangement of the atoms within a molecule of chloral, we must take into consideration the chemical properties and methods of formation of the compound. If chloral is warmed with sodium hydroxide, it is decomposed into chloroform, , and sodium formate, $NaCO_2H$. The formation of chloroform in this way suggests that the three chlorine atoms in chloral are all attached to the same carbon atom, or, in other words, that the structure of the chloral molecule is correctly represented by formula (1). This is supported by a number of other experimental facts. For example, chloral is closely related in chemical properties to a compound called acetaldehyde, and can, in fact, be obtained from acetaldehyde by the action of chlorine. Since acetaldehyde is known, for other reasons, to have the structural formula

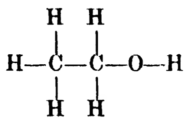


this relationship can be taken as strong evidence for the accepted structural formula of chloral.

The method of writing structural formulæ by drawing lines from the symbol for each element is somewhat cumbersome. The formulæ can be shortened by employing dots instead of lines. In this way the formulæ of water and carbon dioxide can be written

$$H.O.H \text{ and } O:C:O \text{ respectively.}$$

Formulæ may be still further condensed by omitting the valency bonds which join multivalent atoms such as C to univalent atoms such as H. Thus the constitutional formula for ethyl alcohol which is



may be condensed to $CH_3.CH_2.OH$. In writing such formulæ, which are really a kind of chemical shorthand, it is assumed that the univalent atoms are directly attached to the multivalent atom against which they are placed without the intervention of a dot. This will be readily understood by a comparison of the two formulæ given for ethyl alcohol. The process of condensation is sometimes carried to the extent of only separating one particularly active or characteristic group of atoms from the rest of the molecule. Thus, ethyl alcohol is sometimes written simply $C_2H_5.OH$.

Fully expanded structural formulæ, in which all the valency bonds are inserted, are sometimes distinguished from the more condensed forms by the name "graphic" formulæ, but the distinction is of little importance; for so long as a structural formula expresses what is known of the arrangement of the atoms in a molecule, it does all that is required; and whether it is or is not written in graphic form is a matter of convenience, and often depends on the exigencies of space.

Structural formulæ will be found a great help in correlating and committing to memory the enormous number of facts which form the foundation of organic chemistry. It will be found that the subject resolves itself largely into the study of various groups of atoms or "radicles" and the changes which these radicles undergo. From his knowledge of inorganic compounds the student will be already familiar with this idea of radicles; thus groups of atoms such as NH_4-, $-NO_3$, and $-SO_4$ confer on molecules containing them properties which are more or less independent of the nature of the rest of the molecule. In organic chemistry a number of characteristic groups of atoms, containing the element carbon and others, will be met with.

Isomerism.—It frequently happens that two or more different compounds are known, all of which have the same molecular

formula, even though in physical and chemical properties they may show no resemblance to one another. For example, the compounds ethyl alcohol and dimethyl ether both have the molecular formula C_2H_6O. Such compounds are called isomers or isomerides, and the phenomenon itself is known as isomerism. Since the molecules of two isomeric compounds are built up from the same atoms, both in kind and in number, it is obvious that the differences in properties must be due to different arrangements of the atoms within the molecules. For example, ethyl alcohol and dimethyl ether are represented respectively by the formulæ

$$\begin{array}{ccccccc} & & H & & H & & \\ & & | & & | & & \\ H & — & C & — & C & — & O — H \\ & & | & & | & & \\ & & H & & H & & \end{array} \quad \text{and} \quad \begin{array}{ccccccc} & & H & & & H & \\ & & | & & & | & \\ H & — & C & — O — & & C & — H. \\ & & | & & & | & \\ & & H & & & H & \end{array}$$

These formulæ have been selected, as previously pointed out, as a result of a study of the properties and methods of formation of the two compounds, aided by the limitations imposed by considerations of valency. This will be better understood when the two compounds have been studied in some detail. It need only be mentioned here that these structural formulæ express in a concise manner the chemical properties of the two compounds. Thus ethyl alcohol is a very reactive compound, whereas dimethyl ether is comparatively inert, the difference being largely due to the presence in the ethyl alcohol molecule of the very reactive —OH group.

CHAPTER XV

HYDROCARBONS OF THE PARAFFIN SERIES

METHANE, CH_4

A LARGE number of compounds exist which are composed of carbon and hydrogen only, and are known collectively as hydrocarbons. Methane is the simplest member of this class of compounds, and is commonly called *Marsh Gas*, a name which originated from the fact that it is a constituent of the gases arising from marshes and stagnant pools. Methane is formed when coal or wood is strongly heated out of contact with air, a process known as destructive distillation. Ordinary coal gas, which is made from coal in this way, contains about 40 per cent of methane, and the explosive "fire damp" sometimes met with in coal mines consists largely of methane.

Preparation.—(1) It can be made from its elements by heating carbon at about 1200° in an atmosphere of hydrogen :

$$C + 2H_2 = CH_4.$$

This method is only of theoretical interest.

(2) In the laboratory it is generally prepared by heating a mixture of anhydrous sodium acetate and excess of soda-lime :

$$\underset{\text{Sodium acetate.}}{CH_3.COONa} + NaOH = CH_4 + Na_2CO_3.$$

The mixture is strongly heated in a flask made of hard glass, or better, of copper, the gas being collected over water. If very pure methane is required, barium oxide should be substituted for the soda-lime.

(3) Pure methane can be prepared by reducing methyl iodide[1] by means of nascent hydrogen :

$$CH_3I + 2H = CH_4 + HI.$$

The reducing agent usually employed is zinc-copper couple in the presence of 95 per cent alcohol. Zinc-copper couple is simply metallic zinc coated with a thin deposit of copper, and it is

[1] The groups of atoms CH_3-, C_2H_5-, and C_3H_7- are called methyl, ethyl, and propyl respectively (p. 215).

capable of decomposing water or moist alcohol with evolution of hydrogen.

Properties.—Methane is a colourless, odourless gas, insoluble in water, and much lighter than air (density 8·0). It does not liquefy until cooled to $-160°$. It burns in air with a pale blue flame, carbon dioxide and water being produced :

$$CH_4 + 2O_2 = CO_2 + 2H_2O.$$

A mixture of methane and air explodes violently when a light is applied to it.

In most of its chemical properties methane is exceedingly stable and non-reactive. It is unacted on by concentrated acids or alkalies, and is not affected by passing through solutions of such powerful oxidising agents as acidified potassium permanganate or dichromate. When a mixture of methane and chlorine is exposed to diffused sunlight a slow reaction takes place ; the atoms of chlorine gradually displace the hydrogen atoms in the methane molecule, and a mixture of four compounds is formed, the proportion of each depending on the duration of the experiment and on the relative proportions of the reacting substances present :

$$CH_4 + Cl_2 = \underset{\text{Methyl chloride.}}{CH_3Cl} + HCl,$$

$$CH_3Cl + Cl_2 = \underset{\text{Methylene dichloride.}}{CH_2Cl_2} + HCl,$$

$$CH_2Cl_2 + Cl_2 = \underset{\text{Chloroform.}}{CHCl_3} + HCl,$$

$$CHCl_3 + Cl_2 = \underset{\text{Carbon tetrachloride.}}{CCl_4} + HCl.$$

Reactions like this, in which an atom of one element displaces an atom of another element from a molecule, are called reactions of *substitution*, and the product is known as a *substitution product*. It should be noticed that, since carbon is quadrivalent and hydrogen univalent, it is impossible for a methane molecule to add on directly one or more atoms. Such a compound as CH_4Cl, for example, is not known. Compounds like methane, which can only form derivatives by a process of substitution, are said to be *saturated*.

Homologous Series.—Methane is the first member of a series of hydrocarbons called the *paraffins*, which are all very similar in chemical properties.[1] Each member can be considered as being

[1] The word " paraffin " is derived from the Latin *parum affinis*, and should serve to remind the student of the great stability and inertness of the hydrocarbons of this series.

derived from the next lower member by the substitution of the group CH_3- for one of the hydrogen atoms. It follows, therefore, that the molecular formulæ of successive members of the series differ by CH_2, so that the second member will have the formula C_2H_6, and the third C_3H_8. Such a series of compounds is called a homologous series. Many other homologous series will be described later.

The paraffin hydrocarbons show a gradual transition in physical properties from methane upwards. Thus the first four members are gases, then come a number of liquids of gradually rising boiling-point, whilst the hydrocarbon $C_{16}H_{34}$ and those above it are waxy solids. It is a fairly general rule that, in the case of any homologous series, the melting- and boiling-points of the individual compounds rise gradually, though perhaps irregularly, as the series is ascended.

ETHANE, C_2H_6

Ethane is the paraffin hydrocarbon next above methane. Its constitutional formula is

$$\begin{array}{ccccccc} & & H & & H & & \\ & & | & & | & & \\ H & — & C & — & C & — & H \\ & & | & & | & & \\ & & H & & H & & \end{array} \qquad \text{or} \qquad CH_3.CH_3.$$

Preparation.—It can be prepared by methods similar to those employed in the case of methane.

(1) The sodium salt of propionic acid (the next higher member of the series to which acetic acid belongs) yields ethane on strongly heating with soda-lime, just as sodium acetate yields methane :

$$\underset{\text{Sodium propionate.}}{C_2H_5.COONa} + NaOH = C_2H_6 + Na_2CO_3.$$

(2) Ethane can also be prepared by reducing ethyl iodide with zinc-copper couple and moist alcohol :

$$C_2H_5I + 2\hat{H} = C_2H_6 + HI.$$

(3) A third method, which is different from any of those described for methane, consists in treating a methyl halide with metallic sodium. The sodium removes the halogen from two molecules of the methyl halide, and the residual CH_3- groups unite to form a molecule of ethane :

$$CH_3Cl + 2Na = CH_3.CH_3 + 2NaCl.$$

This is an example of an important general reaction—the Würtz reaction—which can be employed for the preparation of most paraffins containing an even number of carbon atoms.

Properties.—Ethane is a colourless gas, which closely resembles methane in physical properties, but can be liquefied much more easily.

Like methane, it is an exceedingly stable compound, and is not acted upon by acids, alkalies, or oxidising agents. In diffused light it slowly reacts with chlorine yielding substitution products, the hydrogen atoms being displaced, one by one, by atoms of chlorine. The final product is hexachlorethane, or carbon hexachloride, C_2Cl_6.

Higher Members of the Paraffin Series

Propane, C_3H_8, is the paraffin next above ethane. It is a gas which closely resembles methane and ethane, and can be prepared by similar methods. Its constitutional formula is :

$$\begin{array}{ccccccc} & & H & & H & & H & & \\ & & | & & | & & | & & \\ H & — & C & — & C & — & C & — & H \\ & & | & & | & & | & & \\ & & H & & H & & H & & \end{array} \quad \text{or} \quad CH_3.CH_2.CH_3.$$

It will be seen on inspection that this formula, like the formulæ previously given for methane and ethane, is the only possible one which satisfies the valency requirements of the various atoms.

The Butanes.—When we come to the next member of the series, C_4H_{10}, we find that two compounds of this molecular formula might be theoretically derived from propane, according as to whether a hydrogen atom attached to one of the end carbon atoms, or one attached to the central carbon atom, is displaced by a CH_3 – group. The two structural formulæ thus obtained are, respectively :

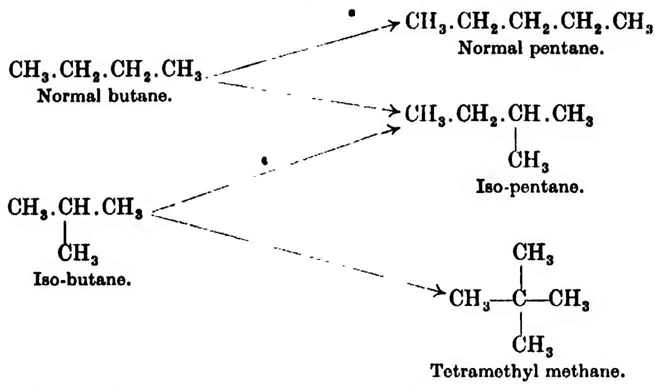
$$\underset{\text{(I.)}}{CH_3.CH_2.CH_2.CH_3} \quad \text{and} \quad \underset{\text{(II.)}}{\begin{array}{c} CH_3.CH.CH_3 \\ | \\ CH_3 \end{array}}$$

As a matter of fact, two compounds of the molecular formula C_4H_{10} are actually known. One of them is prepared by the action of sodium on ethyl iodide, and must therefore be represented by Formula I. :

$$2CH_3.CH_2I + 2Na = CH_3.CH_2.CH_2.CH_3 + 2NaI.$$

Since this compound contains in its molecule a single straight chain of carbon atoms, it is called *normal butane.* The isomeric compound represented by Formula II. is called *iso-butane.*

The Pentanes.—There are three isomeric pentanes of the molecular formula C_5H_{12}. Their derivation from the butanes may be represented as follows :



Normal pentane and iso-pentane occur in petroleum spirit (below).

Higher up the series, the numbers of possible isomers become increasingly great. With the exception of methane, ethane, propane, and the butanes, the names of the paraffins have Greek prefixes showing the number of carbon atoms in the molecule. Thus the next members above the pentanes are:

The hexanes, C_6H_{14} (five isomers).
The heptanes, C_7H_{16} (nine isomers).
The octanes, C_8H_{18} (eighteen isomers).

Petroleum

In many parts of the world, more particularly in Baku on the Caspian Sea, in Pennsylvania, and in Mexico, large quantities of petroleum oil occur in beds beneath the surface of the earth, from which the oil can be pumped. Crude petroleum is a thick brownish liquid, and is largely used as a fuel. American petroleum consists almost entirely of a mixture of higher members of the paraffin series of hydrocarbons, but the oil from Baku consists chiefly of hydrocarbons of a different class.

By fractionally distilling crude petroleum, the oil can be split up into several fractions differing widely in boiling-point, some of which are of considerable importance in pharmacy. It must be remembered that these products are mixtures and not pure compounds, and that different samples may differ appreciably in composition.

Petroleum Spirit is the fraction of lowest boiling-point obtained from crude petroleum, and distils between about 40° and 60°. It is used as a solvent in certain pharmacopœial tests.

Paraffinum Liquidum, *Liquid Paraffin,* is a mixture of hydrocarbons, chiefly of the paraffin series. It is miscible with chloroform, ether, and fixed and volatile oils. It dissolves bromine, iodine,

iodoform, and phosphorus. Its specific gravity lies between 0·860 and 0·890. The viscosity of different samples varies considerably: some idea of the relative viscosities of different samples may be obtained by filling a 25-mil pipette and observing the times taken to run out, at a given temperature (Squire).

Paraffinum Molle, *Soft Paraffin*, is a translucent mixture of semi-solid hydrocarbons. It is insoluble in water, sparingly soluble in absolute alcohol, and easily soluble in ether, chloroform, and benzene. It melts at 42°-46°, and its specific gravity is about 0·820-0·850 at 60°.

Vaseline is the trade name for a soft paraffin prepared by the Chesebrough Manufacturing Company, and which apparently consists of a definite mixture of hydrocarbons. Vaseline is not subject to the variations in composition from which ordinary soft paraffin suffers, and is therefore a more reliable preparation to use when making "stainless" ointments of iodine, since the proportions of iodine which combine with the "unsaturated" hydrocarbons present may be relied upon to be a constant quantity.

Paraffinum Durum, *Hard Paraffin*, is obtained from the products of the destructive distillation of bituminous shale or cannel coal. It is a colourless, wax-like solid, greasy to the touch, and consists of a mixture of solid hydrocarbons of the paraffin series. Its m.p. is about 50°-60° and its specific gravity about 0·90. It is insoluble in water, sparingly soluble in alcohol, and soluble 1-80 in ether.

Other products of commercial importance obtained from crude petroleum include petrol, kerosene, or burning oil, and various qualities of lubricating oils.

CHAPTER XVI

THE UNSATURATED HYDROCARBONS

ETHYLENE, C_2H_4

Preparation.—(1) The gas ethylene is generally prepared by heating ordinary alcohol (ethyl alcohol) with a large excess of concentrated sulphuric acid. The final result is that each molecule of alcohol loses a molecule of water with formation of ethylene :

$$\underset{\substack{\text{Ethyl}\\\text{alcohol.}}}{C_2H_5.OH} = C_2H_4 + H_2O.$$

In reality the reaction takes place in two stages. Alcohol and concentrated sulphuric acid react to form a compound called ethyl hydrogen sulphate :

$$C_2H_5.OH + H_2SO_4 = C_2H_5.HSO_4 + H_2O.$$

This compound, on heating, decomposes into ethylene and sulphuric acid :

$$C_2H_5.HSO_4 = C_2H_4 + H_2SO_4.$$

A mixture of alcohol (40 mils) and concentrated sulphuric acid (150 mils) is heated at about 165° in a litre flask, the temperature being read by means of a thermometer immersed in the liquid. The gas is washed free from sulphur dioxide and other impurities by bubbling through a solution of sodium hydroxide, and is then collected over water. When the evolution of gas ceases, a further supply can be obtained by adding a further quantity of a mixture of alcohol and sulphuric acid through a thistle funnel, which also serves as a safety tube to prevent any possibility of the sodium hydroxide sucking back into the hot acid.

(2) Ethylene may also be prepared by boiling ethyl chloride, bromide, or iodide with a solution of potassium hydroxide in alcohol (commonly known as " alcoholic potash "). Under these conditions the alkali removes a molecule of hydrogen chloride from the ethyl halide, liberating ethylene :

$$C_2H_5Br + KOH = C_2H_4 + KBr + H_2O.$$

Properties.—Ethylene is a colourless gas, of density 14, and has a faint, sweetish odour. It is very sparingly soluble in water, and can be liquefied at ordinary temperatures by the application of great pressure.

In chemical properties ethylene differs entirely from methane or the other paraffin hydrocarbons. It burns in air with a yellow luminous flame. It is an exceedingly reactive gas, and is capable of combining directly with certain other substances. Thus, when a mixture of ethylene and hydrogen is passed over finely divided platinum, ethane is formed :

$$C_2H_4 + H_2 = C_2H_6.$$

When ethylene is bubbled into cold concentrated sulphuric acid it is slowly absorbed, ethyl hydrogen sulphate being produced :

$$C_2H_4 + H_2SO_4 = C_2H_5.HSO_4.$$

Ethylene combines directly with the halogens. Thus if the gas is bubbled into liquid bromine, the colour of the bromine rapidly disappears, and *ethylene dibromide*, a colourless, oily liquid with a pleasant odour, is formed :

$$C_2H_4 + Br_2 = C_2H_4Br_2.$$

Similar compounds are formed with chlorine and with iodine. Ethylene also combines directly with hydrobromic and hydriodic acids,[1] forming ethyl bromide and ethyl iodide respectively :

$$C_2H_4 + HI = C_2H_5I.$$

Ethylene is very readily attacked by oxidising agents. If the gas is bubbled through a neutral, acid, or alkaline solution of potassium permanganate the permanganate is immediately reduced.

Compounds which, like ethylene, are capable of forming derivatives by direct addition, are said to be *unsaturated*, as distinguished from saturated compounds like the paraffins, which can only form derivatives by a process of substitution.

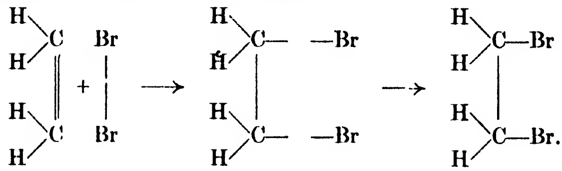
Constitution.—The molecular formula of ethylene is known as a result of analyses and density determinations. Assuming that carbon and hydrogen have their usual valencies, only one constitutional formula is possible, namely :

$$\begin{matrix} H & & & & H \\ & \diagdown & & \diagup & \\ & & C=C & & \\ & \diagup & & \diagdown & \\ H & & & & H \end{matrix} \quad \text{or} \quad CH_2 : CH_2.$$

In order to fulfil the valency conditions, the carbon atoms are represented as being joined together by two valency linkages, or a

[1] It is an interesting fact that ethylene does not combine directly with hydrochloric acid.

"double bond" as it is usually called. When ethylene combines directly with other substances, it is supposed that the double bond is "broken", so that each carbon atom can combine with one univalent atom or group. For example :



This view of the constitution of ethylene is borne out by the fact that in additive reactions a molecule of ethylene always combines with *two* univalent atoms or groups. It is impossible, for instance, to prepare such a compound as $CH_2.CH_2Br$ by the combination of ethylene with bromine.

All unsaturated organic compounds contain one or more double (or treble) bonds. Such compounds can generally be reduced by nascent hydrogen, and can combine directly with halogens and halogen acids with formation of saturated compounds ; they can, invariably, be easily oxidised. Unsaturated compounds may, as a rule, be recognised by the following tests :

(i.) They immediately reduce a cold alkaline solution of potassium permanganate, hydrated manganese dioxide being precipitated.

(ii.) They combine directly with liquid bromine.

(iii.) They rapidly decolorise bromine water, which acts as an oxidising agent :

$$Br_2 + H_2O = 2HBr + \hat{O}.$$

A double bond in a molecule has no mechanical significance. It must not be thought that carbon atoms joined by a double bond are more firmly held together than those joined by a single bond : indeed, the reverse is the case, since oxidation of an unsaturated compound results in the molecule being split up or disrupted at the double bond.

These remarks apply only to compounds having double bonds between one carbon atom and another. Compounds in which a carbon and a nitrogen atom, a carbon and an oxygen atom, or two nitrogen atoms are joined by a double bond do not, as a rule, show the behaviour of ordinary unsaturated compounds.

The Olefines.—Ethylene is the first member of a series of hydrocarbons called the olefines, each of which contains two atoms of hydrogen less than the corresponding paraffin. The other olefines are all very similar in chemical properties to ethylene, and can be prepared by similar methods. The next higher member is *propylene*,

$CH_3.CH:CH_2$. It is a colourless gas which combines directly with the halogens and reduces alkaline permanganate in the cold. It can be prepared by heating propyl alcohol, $C_3H_7.OH$, with concentrated sulphuric acid, or by boiling propyl bromide with alcoholic potash:

$$C_3H_7.OH = C_3H_6 + H_2O,$$
$$C_3H_7Br + KOH = C_3H_6 + KBr + H_2O.$$

There are three isomeric *butylenes*, namely:

$CH_3.CH_2.CH:CH_2$.
Normal butylene or ethyl ethylene.

$CH_3.CH:CH.CH_3$.
β-butylene or symmetrical dimethyl ethylene.

$(CH_3)_2C:CH_2$.
Iso-butylene or unsymmetrical dimethyl ethylene.

In the case of each of these compounds the second name given is preferable to the first, since it expresses more clearly the constitution of the compound and its relationship to ethylene.

It should be noted that no olefine of the formula CH_2, corresponding to methane, is known. Such a compound would contain, not a double bond, but a bivalent carbon atom, and experience has shown that such compounds cannot be prepared. The name "methylene" is, however, applied to the group of atoms $>CH_2$.

Acetylene, C_2H_2

Acetylene is a gas of great industrial importance, and is largely used as an illuminant. It is not an olefine, but is the lowest member of another series of unsaturated hydrocarbons.

Preparation.—(1) Acetylene is formed in small quantities from its elements when an electric arc is passed between carbon poles in an atmosphere of hydrogen. It is also formed when coal gas burns in an insufficient supply of air, as, for example, when a bunsen burner is lit at the bottom of the tube.

(2) Acetylene is formed when ethylene dichloride (or dibromide or di-iodide) is boiled with alcoholic potash:

$$C_2H_4Br_2 + 2KOH = C_2H_2 + 2KBr + 2H_2O.$$

This is perfectly analogous to the preparation of ethylene from ethyl bromide.

(3) Acetylene is always prepared in practice by the action of water on calcium carbide. Calcium carbide is a hard, grey solid, and is manufactured by heating a mixture of coke and lime in an electric furnace:

$$CaO + 3C = CaC_2 + CO.$$

On treatment with water in the cold it is decomposed with evolution of acetylene :

$$CaC_2 + 2H_2O = C_2H_2 + Ca(OH)_2.$$

For the preparation of the gas in the laboratory, the lumps of calcium carbide are placed in a flask and covered with a layer of sand. Water is added drop by drop from a dropping funnel, and the gas evolved is collected over water. The object of the layer of sand is to make the water percolate slowly through to the carbide, so that the gas is given off steadily and not in irregular rushes.

Properties.—Acetylene is a colourless gas with an unpleasant, very characteristic smell. It is slightly soluble in water. The gas burns in air in the ordinary way with a smoky yellow flame, but by the use of special burners the flame can be made smokeless and very brilliant. A mixture of acetylene and air explodes violently when a flame is applied.

In chemical properties acetylene resembles the olefines in that it is highly unsaturated. Thus it combines with hydrogen in the presence of platinum black to form ethane :

$$C_2H_2 + 2H_2 = C_2H_6.$$

It combines directly with the halogens, the reaction taking place in two stages. For example :

$$\text{(i.)}\ C_2H_2 + Cl_2 = C_2H_2Cl_2.$$
$$\text{(ii.)}\ C_2H_2Cl_2 + Cl_2 = C_2H_2Cl_4.$$

These facts, together with considerations of valency, show that acetylene must be represented by the structural formula $CH \equiv CH$ or $CH \vdots CH$, the carbon atoms being linked together by a "treble bond". All compounds containing such a treble linkage resemble acetylene in that they can combine with either two or four univalent atoms or groups, the valency bonds being always saturated in pairs.

Copper acetylide, Cu_2C_2, is formed as a dark red precipitate when acetylene is passed into an ammoniacal solution of cuprous chloride. The dried compound explodes violently if heated or if struck with a hammer. On treatment with hydrochloric acid it yields acetylene.

Silver acetylide, Ag_2C_2, formed when acetylene is passed into an ammoniacal solution of silver nitrate, is even more explosive than the copper compound.

CHAPTER XVII

THE MONOHYDRIC ALCOHOLS

MENTION has already been made of the groups of atoms: methyl, ethyl, propyl, etc. These are known collectively as the *alkyl radicles*, and may be considered as being theoretically derived from the corresponding paraffins by the removal of a hydrogen atom. For example:

Methyl, CH_3—	derived from	methane, CH_4.
Ethyl, $CH_3.CH_2$—	,, ,,	ethane, $CH_3.CH_3$.
Propyl, $CH_3.CH_2.CH_2$—	,, ,,	propane, $CH_3.CH_2.CH_3$.
Iso-propyl, $(CH_3)_2CH$—	,, ,,	,, ,,

These radicles are of course only met with in combination, and are no more capable of existing in the free state than are such inorganic radicles as NH_4-, $-SO_4$, and $-NO_3$.

Alcohols are a class of compounds which contain the hydroxyl group, $-OH$, combined with an alkyl radicle, and they may be regarded therefore as the hydroxides of the alkyl radicles. They form a homologous series, the lowest number of which is methyl alcohol, $CH_3.OH$.

METHYL ALCOHOL, $CH_3.OH$

Preparation.—(1) Methyl alcohol can be made synthetically[1] by heating a methyl halide with water or with dilute alkalies under pressure:

$$CH_3Cl + H_2O = CH_3.OH + HCl.$$

This method is only of theoretical interest.

(2) All the methyl alcohol of commerce is obtained by the destructive distillation of wood in iron retorts, the temperature being gradually raised during several hours. At first, gases, chiefly carbon monoxide and hydrogen, are evolved, but as the temperature increases a tarry liquid collects in the receivers. The heating is

[1] A synthetic process is one by which a compound is built up from its elements, or from simpler compounds which can themselves be built up from their elements. In this particular case the methyl chloride could be made from carbon, hydrogen, and chlorine by the following series of reactions:

$$C + 2H_2 \xrightarrow[\text{at } 1200°]{} CH_4 \xrightarrow[\text{action of chlorine}]{} CH_3Cl.$$

continued until all the volatile decomposition products of the wood have distilled over, and nothing remains in the retorts but a mass of wood-charcoal. The distillate, on settling, separates into two layers:

(i.) Wood tar.[1]

(ii.) A brownish, aqueous layer known as "pyroligneous acid", which contains about 10 per cent of acetic acid (p. 243), 2 per cent of methyl alcohol, and 0·5 per cent of acetone (p. 240).

The pyroligneous acid is separated and distilled, and the vapours are passed through hot milk of lime, which "fixes" the acetic acid as its calcium salt. The methyl alcohol, together with acetone, water, and other impurities, passes on, and is condensed in a receiver. The distillate is decolorised by filtration through animal charcoal, and is then fractionally distilled to get rid of most of the water, the last traces of which are removed by adding quicklime and again distilling. The methyl alcohol obtained in this way still contains acetone and traces of other impurities, from which it is freed by mixing with anhydrous calcium chloride, with which methyl alcohol forms a solid compound, $CaCl_2.4CH_3OH$. This solid is pressed to remove liquid (acetone, etc.), and is then decomposed by distillation with water. The methyl alcohol in the distillate is freed from water by fractional distillation, followed by distillation over quicklime.

Properties.—Methyl alcohol is a colourless liquid (specific gravity 0·80, and b.p. 66°), having a characteristic alcoholic odour and a burning taste. It mixes in all proportions with water and with ethyl alcohol, and burns with a pale blue flame, with formation of water and carbon dioxide.

Chemically, methyl alcohol is a very reactive compound. A piece of metallic sodium added to the liquid dissolves, with evolution of hydrogen. If now the excess of methyl alcohol is evaporated off, an "alcoholate" called *sodium methoxide* remains, a sodium atom having displaced the hydrogen atom from the $-OH$ group:

$$2CH_3.OH + 2Na = 2CH_3.ONa + H_2.$$

Sodium methoxide is a hygroscopic solid, and is at once decomposed by water with regeneration of the alcohol:

$$CH_3.ONa + H_2O = CH_3.OH + NaOH.$$

Potassium reacts with methyl alcohol in a similar manner.

Methyl alcohol is neutral to litmus, although in some ways it behaves like a very weak basic hydroxide. Thus, if dry hydrogen

[1] **Pix Liquida,** *Tar,* is the tar obtained in this way from various species of Pinus. It is dark brown or black, and of a semi-liquid consistency. Chemically, it is a complex mixture of hydrocarbons, phenols (p. 346), and other compounds.

Creosotum, *Creosote,* is a colourless or pale yellow liquid obtained by fractional distillation of beechwood tar. It consists mainly of creosol and guaiacol (p. 352).

chloride gas be passed into dry methyl alcohol, methyl chloride is produced, a reaction which may be compared with the neutralisation of ammonium or sodium hydroxides with hydrochloric acid :

$$CH_3.OH + HCl = CH_3Cl + H_2O,$$
$$NH_4.OH + HCl = NH_4Cl + H_2O.$$

The analogy between the two cases is in reality very slight. The reaction between ammonium hydroxide and hydrochloric acid takes place instantaneously and completely, even in dilute solution ; but in the case of methyl alcohol and hydrogen chloride the reaction is slow, and never proceeds quite to completion, owing to the fact that it is reversible, the water produced during the reaction tending to reconvert the methyl chloride into methyl alcohol :

$$CH_3Cl + H_2O \rightleftharpoons CH_3.OH + HCl.$$

Other acids, both organic and inorganic, react with methyl and other alcohols in a similar way. The products formed are called " ethereal salts " or " esters ", so that methyl chloride, for example, may be said to be the methyl ester of hydrochloric acid. The process of conversion of an acid into an ester by interaction with an alcohol is called " esterification ". The reverse process, the splitting up of an ester into a mixture of an alcohol and an acid by means of water, is called " hydrolysis ". The preparation of some of the more important esters will be described later.

Methyl alcohol is readily acted on by phosphorus tri- or penta-chloride, with formation of methyl chloride :

$$CH_3.OH + PCl_5 = CH_3Cl + POCl_3 + HCl.$$

The bromides and iodides of phosphorus behave similarly.

Methyl alcohol is readily converted by oxidising agents, such as acidified potassium dichromate solution, into formaldehyde. This, on further oxidation, passes into formic acid :

$$CH_3.OH + O = \underset{\text{Formal-dehyde.}}{H.CHO} + H_2O,$$

$$H.CHO + O = \underset{\text{Formic acid.}}{H.COOH}.$$

Constitution.—The accepted constitutional formula for methyl alcohol

$$\begin{array}{c} \text{H} \\ | \\ \text{H—C—O—H} \\ | \\ \text{H} \end{array} \quad \text{or} \quad CH_3.OH$$

is the only possible formula which satisfies the valency conditions of the various atoms. It agrees well with the chemical properties of the compound. Thus, only one hydrogen atom can be displaced

from the methyl alcohol molecule by sodium, showing that one hydrogen atom is in a different state of combination from the other three. Further, the oxygen atom and one of the hydrogen atoms can be together displaced from the molecule by *one* chlorine atom (by the action of phosphorus pentachloride), a reaction which is readily understood if we assume that the methyl alcohol molecule contains the univalent —OH group.

Tests for Methyl Alcohol.—(1) Hold a hot spiral of platinum wire over some warm methyl alcohol contained in a beaker. The wire becomes red-hot, and the characteristic odour of formaldehyde is evolved.

(2) To about 2 mils of the sample add about 1 mil of glacial acetic acid and 2 mils of concentrated sulphuric acid, and warm. A pleasant odour of methyl acetate, closely resembling that of ethyl acetate, is evolved.

(3) Methyl alcohol does not give the iodoform reaction (p. 221, Distinction from ethyl alcohol and acetone).

(4) Methyl alcohol can be detected, either alone or in the presence of ethyl alcohol, as described on p. 224.

Ethyl Alcohol, $CH_3.CH_2.OH$

Ethyl alcohol is the ordinary "alcohol" of commerce, and occurs in wines, beer, spirits, and all fermented liquors. It is one of the most important of all organic compounds, being extensively used as a solvent and as a starting-point for the preparation of other compounds.

Preparation.—(1) Ethyl alcohol can be prepared by a method similar to that described for methyl alcohol, namely, by boiling an ethyl halide with water, or, preferably, with a dilute solution of an alkali:[1]

$$C_2H_5Br + H_2O = C_2H_5.OH + HBr.$$

(2) Alcohol can be prepared in the laboratory, in small quantities, by the fermentation of a solution of ordinary cane sugar.

About 500 mils of dilute (5 per cent) sugar solution is set aside in a warm place, and a small quantity of fresh brewer's yeast added. After a short time the mixture begins to froth and evolve carbon dioxide, at the same time acquiring a characteristic odour resembling that of beer. After a day or two the liquid is distilled, only about the first 150 mils of the distillate, containing most of the alcohol, being collected. The product can be freed from water by fractional

[1] This provides a method by which ethyl alcohol can be synthesised from its elements. The complete series of reactions is as follows:

$$C + 2H_2 \xrightarrow[\text{at } 1200^\circ]{} CH_4 \xrightarrow[\text{action of chlorine}]{} CH_3Cl$$
$$\xrightarrow[\text{action of sodium}]{} CH_3.CH_3 \xrightarrow[\text{action of chlorine}]{} CH_3.CH_2Cl$$
$$\xrightarrow[\text{action of aqueous alkalies}]{} CH_3.CH_2.OH.$$

distillation followed by distillation over quicklime, and in this way alcohol containing less than 1 per cent of water is obtained, this constituting the Absolute Alcohol of the Pharmacopœia.

The fermentation of sugar solutions is due to the presence in the yeast of certain substances known as enzymes. Enzymes are lifeless, nitrogenous, amorphous, soluble substances of complex composition, which occur in the cell juices of certain plants. They are capable of bringing about certain chemical changes, the effect being comparable with that of inorganic catalysts. The following important points about enzyme action should be noted:

(i.) A particular enzyme can only, as a rule, bring about one particular type of chemical reaction.

(ii.) Like many inorganic catalysts, an enzyme slowly loses its activity during the reaction.

(iii.) The catalytic activity of an enzyme is destroyed by heat.

Yeast is a unicellular plant which contains in its cell sap three important enzymes: (i.) maltase, which can convert maltose (malt sugar) into a mixture of glucose and fructose; (ii.) invertase, which can convert cane sugar into a mixture of glucose and fructose; and (iii.) zymase, which can convert either glucose or fructose into alcohol and carbon dioxide. In the formation of alcohol from cane sugar solution, only the last two of these enzymes take part. The reaction takes place in two stages:

Action of invertase—

$$\underset{\text{Cane sugar.}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Glucose.}}{C_6H_{12}O_6} + \underset{\text{Fructose.}}{C_6H_{12}O_6}.$$

Action of zymase—

$$\underset{\substack{\text{Glucose or}\\ \text{fructose.}}}{C_6H_{12}O_6} = 2C_2H_5.OH + 2CO_2.$$

Manufacture.—Alcohol can be prepared on the large scale by the fermentation of products rich in sugar, such as molasses or the juice of the sugar beet.

The greater part of the alcohol of commerce is made from potatoes and corn, which provide cheap sources of starch. The starch is first converted into sugars, which are then made to undergo alcoholic fermentation. A brief description of the usual process is as follows:

Moistened barley is kept at a gentle heat until the grain commences to germinate, the product being "malt". During germination an enzyme, diastase, is produced, after which further germination is arrested by drying the malt at a temperature of about 50°. The diastase is capable of converting the starch in the barley into maltose; but, as the amount of diastase produced is sufficient to convert much more starch than the barley contains, a cheaper source of starch, such as potatoes or maize, is mixed with the malt, the whole being ground in a mill.

From the mill the mixture is led into a " mash-tun ", where it is mixed with water and maintained at a temperature of 60° for some time, with constant agitation. During this time the diastase converts the whole of the starch present into maltose.

The liquid (now known as the " wort ") is run off, cooled, and fermented by the addition of about 2 per cent of yeast, the fermentation taking from three to nine days. The vat is covered towards the end of the time to prevent " souring " by oxidation of the alcohol to acetic acid. The whole process may be summarised as follows :

$$\text{Starch} \xrightarrow[\text{(Diastase.)}]{} \text{Maltose.}$$

$$\text{Maltose} \xrightarrow[\text{(Maltase.)}]{} \begin{cases}\text{Glucose.}\\ \text{Fructose.}\end{cases}$$

$$\left.\begin{matrix}\text{Glucose}\\ \text{Fructose}\end{matrix}\right\} \xrightarrow[\text{(Zymase.)}]{} \begin{cases}\text{Alcohol.}\\ CO_2.\end{cases}$$

When a concentration of 13 to 15 per cent is reached the fermentation ceases, owing to the inhibitory action of the alcohol on the enzymes. The liquid is then fractionally distilled, the product being an 80 to 90 per cent alcohol, containing traces of amyl and other higher alcohols, together known as " fusel oil ", from which it must be freed. The impure alcohol is poured into water, which throws the fusel oil out of solution in the form of minute oily drops. The liquid is filtered through animal charcoal, which retains most of the fusel oil, and is then fractionally distilled, being finally dried over quicklime and again distilled to yield absolute alcohol.

Properties.—Alcohol is a colourless, mobile liquid (specific gravity 0·786 at 25°, b.p. 78°), which does not solidify until − 130°. It has a characteristic odour, a burning taste, and is very inflammable, burning with a non-luminous flame to form carbon dioxide and water.

The chemical properties of alcohol are so similar to those of methyl alcohol that it is only necessary to mention them briefly. When treated with metallic sodium or potassium, hydrogen is evolved, and the metal dissolves to form sodium or potassium ethoxide, $2C_2H_5.OH + 2K = 2C_2H_5.OK + H_2$. These ethoxides are similar in properties to the corresponding methoxides.

Alcohol reacts with acids, in the absence of water, to form esters ; for example :

$$C_2H_5.OH + HBr = C_2H_5Br + H_2O.$$

When alcohol is mixed with concentrated sulphuric acid, the acid ester, ethyl hydrogen sulphate, is produced. This compound has been previously mentioned in connection with the preparation of ethylene :

$$C_2H_5.OH + H_2SO_4 = C_2H_5.HSO_4 + H_2O.$$

Chlorides, bromides, or iodides of phosphorus convert alcohol into the corresponding ethyl halides; for example:

$$3C_2H_5.OH + PCl_3 = 3C_2H_5Cl + H_3PO_3.$$

Alcohol is readily oxidised by a warm acidified solution of potassium dichromate, with formation of acetaldehyde. This on further oxidation is converted into acetic acid:

$$C_2H_5.OH + O = \underset{\substack{\text{Acet-}\\\text{aldehyde.}}}{CH_3.CHO} + H_2O,$$

$$CH_3.CHO + O = \underset{\text{Acetic acid.}}{CH_3.COOH}.$$

Constitution.—Assuming that the atoms have their usual valencies, the constitutional formula of ethyl alcohol must be either

$$\begin{array}{ccccccc} & H & & H & & & \\ & | & & | & & & \\ H- & C & - & C & -O-H & & \\ & | & & | & & & \\ & H & & H & & & \end{array} \quad \text{or} \quad \begin{array}{ccccc} & H & & H & \\ & | & & | & \\ H- & C & -O- & C & -H. \\ & | & & | & \\ & H & & H & \end{array}$$

(I.) (II.)

Since its formation from an ethyl halide (p. 218) is similar to the formation of methyl alcohol from a methyl halide, Formula (I.) seems to be the more acceptable. This view is supported by the following facts:

(i.) One hydrogen atom only is displaceable by sodium or potassium, showing that it is in a different state of combination from the other five.

(ii.) By the action of phosphorus pentachloride, the oxygen atom and one hydrogen atom are together displaced by a single atom of chlorine, pointing to the probability that the molecule contains a univalent —OH group. This is confirmed by the fact that alcohol can be converted into esters in a somewhat similar manner to that whereby metallic hydroxides are converted into salts.

(iii.) Formula (I.) agrees well with the behaviour of alcohol on oxidation.

(iv.) Another compound is known (dimethyl ether, p. 228), the properties and modes of formation of which agree well with Formula (II.).

It will be seen that the reactions of alcohol are largely dependent upon the presence of the —OH group, a fact which is true of the higher members of the series.

Tests for Ethyl Alcohol.—(1) Dilute a few drops of alcohol with about 2 mils of water. Add a few small crystals of iodine, warm gently, and add aqueous sodium carbonate until the brown colour of the iodine disappears. On cooling, a pale yellow crystalline precipitate of iodoform is produced. If very little alcohol is present the iodoform may not be precipitated, but its very characteristic

odour may be observed. Care should be taken not to use too much alcohol or the iodoform will remain in solution in the excess. This test serves to distinguish ethyl from methyl alcohol, but it is also given by acetone and a few other substances.

(2) Add a few drops of alcohol to a solution of potassium dichromate acidified with dilute sulphuric acid, and warm. The solution changes from orange to green, and the characteristic odour of acetaldehyde can be observed.

(3) To about 2 mils of alcohol add about 1 mil of glacial acetic acid and 2 mils of concentrated sulphuric acid, and warm gently. The pleasant, fruity odour of ethyl acetate will be noticed (p. 259).

SPIRITUS RECTIFICATUS

Alcohol (90 per cent). *Syn.* Rectified Spirit

This is an aqueous solution containing in 100 parts by volume 90 parts by volume of ethyl alcohol, corresponding to 85·68 per cent of ethyl alcohol by weight. Specific gravity, 0·8337.

Preparation.—It is prepared from starch- or sugar-containing substances by the method previously described for absolute alcohol, except that the purified aqueous alcohol, instead of being dried over quicklime, is fractionally distilled to bring it up to the required strength.

Tests for Impurities. *Non-volatile Matter.*—It should leave no residue on evaporation.

Oily or Resinous Substances.—No opalescence should be produced on mixing with water. An apparent opalescence, disappearing on standing, may be due to air-bubbles.

Fusel Oil and Allied Impurities.—Pour a few drops on to a clean filter-paper and allow to evaporate. No unpleasant odour should remain.

Amyl Alcohol and other Reducing Impurities (Limit of).—To 100 mils add 2 mils of N/10 silver nitrate, expose to bright light for twenty-four hours, and decant from the black powder which has been formed. The clear liquid thus obtained should undergo no further change when again exposed to light with more N/10 silver nitrate.

Aldehyde (Limit of).—When mixed with half its volume of a 1-5 aqueous solution of sodium hydroxide, the mixture should not immediately darken in colour.

Tannin, Excess of Aldehyde, and other Organic Impurities.—No immediate darkening in colour should be caused by the addition of Solution of Ammonia.

Alcohol Absolutum. *Absolute Alcohol.*—This consists of ethyl alcohol with not more than 1 per cent of water. It is obtained by dehydration of aqueous alcohol and subsequent distillation, as has already been described. Specific gravity, 0·794-0·7969.

Tests for Impurities.—It should be free from the impurities indicated under Spiritus Rectificatus. In addition, the Pharmacopœia prescribes the following test for water:

Anhydrous copper sulphate, shaken occasionally during two or three hours in a well-closed vessel with about fifty times its weight of Absolute Alcohol, should not assume a decidedly blue colour (absence of excess of water).

The Diluted Alcohols.—Made by mixing together alcohol and water, the Pharmacopœia includes four strengths of alcohol other than 90 per cent, namely, 70 per cent, 60 per cent, 45 per cent, and 20 per cent. When alcohol and water are mixed three phenomena will be observed: first, the appearance of tiny air-bubbles due to the fact that air is more soluble in alcohol than in water, and is expelled on dilution; secondly, heat is generated, owing to the formation of a hydrate; and, thirdly, contraction in volume takes place due to the same cause, the contraction being greatest when the proportions are one molecule of $C_2H_5.OH$ to three of H_2O. It will therefore be seen why the Pharmacopœia states that when a mixture of alcohol and water is prescribed the cooled liquid must be employed.

If we desire to find in what proportions one strength of alcohol is to be mixed with water to produce a required strength, a simple method is available.

Example: Mixing 90 per cent with water to yield 70 per cent.
90 per cent loses 20,
Water gains 70,

$\therefore$ take $\left.\begin{array}{l}7 \text{ parts of 90 per cent} \\ 2 \quad ,, \quad \text{water}\end{array}\right\}$ for each 9 parts required.

If we take 1000 mils of alcohol, as in the Pharmacopœia, we require

$$\frac{2 \times 1000}{7} = 285 \text{ mils (approx.) of water.}$$

But the Pharmacopœia says 310·5 mils of water is necessary, because the contraction in volume has been allowed for. We should find that 1000 mils of alcohol and 285 mils of water would not produce 1285 mils of mixture, but less, and we should have to add some 25 mils of water to correct the final volume. This is a fact that must be carefully noticed, and it will be a useful exercise for the student to work out the theoretical quantities for the other diluted alcohols and compare them with the quantities ordered by the Pharmacopœia.

Proof Spirit.—This was official in the 1885 Pharmacopœia under the title of Spiritus Tenuior. It is defined by Act 58 George III. as being such that at a temperature of 51° F. shall weigh exactly $\frac{12}{13}$ths of the weight of an equal measure of distilled water. That is to say, it has a specific gravity of 0·91976 at 15·5° C. It contains 57·10 per cent by volume, or 49·28 per cent by weight, of ethyl alcohol. This concentration was originally fixed as being the most

dilute aqueous alcohol which, on being poured on to gunpowder and ignited, would fire the powder. If the spirit contained more water, the gunpowder was too wet to fire.

For Excise purposes, weaker spirits are termed under-proof (u.p.), and stronger spirits over-proof (o.p.). "20 degrees over-proof" means that 100 volumes of the spirit, diluted with water, yield 120 volumes of proof spirit. "30 degrees under-proof" means that 100 volumes of the spirit contain 70 volumes of proof spirit.

The strength of alcohol solutions can be determined by finding the specific gravity by means of a hydrometer or a specific-gravity bottle. The strength of alcohol which corresponds to the observed specific gravity can then be found by reference to alcoholimetric tables, several of which have been published.

Denatured Alcohol.—For pharmaceutical and industrial purposes, alcohol which has been rendered unfit for drinking by the addition of certain specified substances may be employed by licensed persons, and can be obtained by them free from Excise duty.

Ordinary *methylated spirit* (mineralised spirit) has, at the time of writing, the following composition:

Spirit (60° over-proof) . . .	90 per cent.
Wood naphtha (wood spirit) . .	$9\frac{1}{2}$,,
Crude pyridine	$\frac{1}{2}$,,
Mineral naphtha (petroleum) . .	$\frac{3}{8}$ of 1 per cent by volume.
Methyl violet	Not less than 0·025 oz. per 100 gallons.

The methyl violet is added for colouring purposes. The other impurities give to the spirit an exceedingly disagreeable taste. Methylated spirit can be sold by retailers, and may be used in the preparation of certain liniments of the Pharmacopœia, provided that they are labelled "Methylated". It must not be used for any preparation which might be employed for internal use.

For certain industrial purposes, partially denatured alcohols (consisting of spirit adulterated with wood naphtha only) may be used, but these cannot be sold retail.

Detection of Methylated Spirit in Tinctures and other Alcoholic Liquids.—Distil the liquid until about 5 mils have been collected. Place the distillate in a small distillation flask, add about 6 grammes of potassium dichromate and 50 mils of dilute sulphuric acid. Allow to stand for fifteen minutes and distil off the bulk of the liquid into a small flask kept cold by immersion in water. In this way the ethyl alcohol is oxidised to acetaldehyde and partly to acetic acid; the methyl alcohol is oxidised first to formaldehyde and then to formic acid. Neutralise the final distillate with sodium carbonate, and concentrate by boiling until all aldehydes have been expelled. The solution will now contain sodium acetate and possibly sodium formate. Acidify slightly with acetic acid, add silver nitrate, and warm for a few minutes. A distinct, finely

divided black precipitate indicates the presence of formate, showing that the original liquid contained methyl alcohol.

Higher Alcohols

Classification of Alcohols.—As has already been mentioned, all the monohydric alcohols are similar in chemical properties in so far as their properties are dependent upon the presence in the molecule of the —OH group. In one important respect, namely, their behaviour on oxidation, some alcohols differ widely from others, and alcohols may be divided into three classes according to the products they yield on oxidation.

Primary alcohols, to which class methyl and ethyl alcohols belong, contain the group $—CH_2.OH$ combined with an alkyl radicle (in the case of methyl alcohol with a hydrogen atom). On oxidation they are converted into aldehydes containing the group —CHO, and further oxidation converts the aldehyde into an acid containing the group —COOH :

$$\underset{\text{Ethyl alcohol.}}{CH_3.CH_2.OH} \longrightarrow \underset{\text{Acetaldehyde.}}{CH_3.C\Big\langle^{H}_{O}} \longrightarrow \underset{\text{Acetic acid.}}{CH_3.C\Big\langle^{OH}_{O}.}$$

Secondary alcohols contain the group $>CH.OH$, to which are joined two alkyl groups. On oxidation they yield compounds called ketones, which contain the group $>CO$ joined to two alkyl groups :

$$\underset{\text{Secondary butyl alcohol.}}{\begin{array}{l}CH_3.CH_2\diagdown\\ \qquad\qquad CH.OH\\ CH_3\diagup\end{array}} \longrightarrow \underset{\text{Methyl ethyl ketone.}}{\begin{array}{l}CH_3.CH_2\diagdown\\ \qquad\qquad C\ \ O.\\ CH_3\diagup\end{array}}$$

Tertiary alcohols contain the group $\rangle\!\!—C.OH$ joined to three alkyl groups. They are only oxidised with difficulty, the molecule being usually broken up with formation of a number of oxidation products, all of which contain fewer carbon atoms in the molecule than the original alcohol. As an example may be mentioned tertiary butyl alcohol, $\begin{array}{l}CH_3\diagdown\\ CH_3—C.OH\\ CH_3\diagup\end{array}$, which when oxidised yields a mixture of acetone, $(CH_3)_2CO$, acetic acid, $CH_3.COOH$, carbon dioxide, and other substances.

Propyl alcohol, $CH_3.CH_2.CH_2.OH$, is found in fusel oil, and is a colourless liquid very similar in properties to ethyl alcohol. It boils at 97°, and mixes with water in all proportions. It is a primary alcohol, and yields on oxidation with acidified potassium dichromate solution, first propaldehyde, $CH_3.CH_2.CHO$, and then propionic acid $CH_3.CH_2.COOH$.

Isopropyl alcohol, *$(CH_3)_2CH.OH$, is a secondary alcohol.* It can be prepared by heating isopropyl iodide, *$(CH_3)_2CHI$,* with *silver hydroxide.*

$$(CH_3)_2CHI + AgOH = (CH_3)_2CH.OH + AgI.$$

On oxidation it yields acetone (dimethyl-ketone):

$$(CH_3)_2CH.OH + O = (CH_3)_2CO + H_2O.$$

There are four isomeric **butyl alcohols** of the molecular formula $C_4H_9.OH$, and eight alcohols of the formula $C_5H_{11}.OH$. These latter are called **amyl alcohols.** Fusel oil consists chiefly of *isoprimary amyl alcohol,* $(CH_3)_2CH.CH_2.CH_2.OH$, together with smaller quantities of *optically active amyl alcohol,* $\begin{matrix} CH_3 \diagdown \\ \quad\quad\quad\quad CH.CH_2.OH, \\ CH_3.CH_2 \diagup \end{matrix}$ and other alcohols. Commercial amyl alcohol is prepared from fusel oil by shaking it with a saturated solution of common salt, separating the oily layer, distilling it, and collecting the fraction passing over between 125° and 143°. Mixed with benzene, it is employed under the name of "benzolated amylic alcohol" as a solvent in the extraction of cinchona alkaloids. The amyl alcohols, unlike the lower members of the series, are only sparingly soluble in water. This fact explains why the fusel oil in crude alcohol is thrown out of solution on dilution.

Some of the higher alcohols, notably *cetyl alcohol,* $C_{16}H_{33}.OH$; *ceryl alcohol,* $C_{26}H_{53}.OH$; and *miricyl alcohol,* $C_{30}H_{61}.OH$, occur, in the form of their esters, as the main constituents of waxes (p. 277).

THIO-ALCOHOLS

A number of compounds are known which are similar in structure to the alcohols, except that they contain a sulphur atom in place of the oxygen atom. They are known as thio-alcohols, or more commonly as mercaptans.

Mercaptan, ethyl mercaptan, $C_2H_5.SH$, can be prepared by the action of potassium hydrosulphide, KSH, on ethyl bromide:

$$C_2H_5Br + KSH = C_2H_5.SH + KBr,$$

with which compare:

$$C_2H_5Br + KOH = C_2H_5.OH + KBr.$$

It is a volatile liquid boiling at 36°, and has a disgusting odour recalling that of garlic.

When treated with sodium, mercaptan yields sodium mercaptide, $C_2H_5.SNa$, analogous to sodium ethoxide, $C_2H_5.ONa$. Potassium reacts in a similar way. Mercuric mercaptide, $(C_2H_5.S)_2Hg$, can be prepared by shaking mercaptan with mercuric oxide.

Sulphonal, *Sulphonal,* is an important mercaptan derivative. Ethyl mercaptan reacts with acetone (p. 240) in the presence of hydrogen chloride to form a compound called *mercaptol*:

$$\begin{array}{l}CH_3\diagdown\\ \qquad\quad CO\\ CH_3\diagup\end{array} + 2C_2H_5.SH = \begin{array}{l}CH_3\diagdown\quad\diagup S.C_2H_5\\ \qquad\quad C\\ CH_3\diagup\quad\diagdown S.C_2H_5\end{array} + H_2O.$$

Mercaptol.

Mercaptol, on oxidation with potassium permanganate, yields sulphonal:

$$\begin{array}{l}CH_3\diagdown\quad\diagup S.C_2H_5\\ \qquad\quad C\\ CH_3\diagup\quad\diagdown S.C_2H_5\end{array} + 4O \longrightarrow \begin{array}{l}CH_3\diagdown\quad\diagup SO_2.C_2H_5\\ \qquad\quad C\\ CH_3\diagup\quad\diagdown SO_2.C_2H_5.\end{array}$$

Sulphonal.

Sulphonal forms colourless crystals melting at 125°. It is slightly soluble in alcohol, very sparingly in water, forming neutral solutions.

Methylsulphonal, *Methylsulphonal,* sometimes known as *trional,* is prepared in a similar manner, using methyl ethyl ketone, $\begin{array}{l}CH_3\diagdown\\ \qquad\quad CO\\ C_2H_5\diagup\end{array}$, instead of acetone.

$$\begin{array}{l}CH_3\diagdown\\ \qquad\quad CO\\ C_2H_5\diagup\end{array} \longrightarrow \begin{array}{l}CH_3\diagdown\quad\diagup S.C_2H_5\\ \qquad\quad C\\ C_2H_5\diagup\quad\diagdown S.C_2H_5\end{array} \longrightarrow \begin{array}{l}CH_3\diagdown\quad\diagup SO_2.C_2H_5\\ \qquad\quad C\\ C_2H_5\diagup\quad\diagdown SO_2.C_2H_5.\end{array}$$

Methylsulphonal.

Methylsulphonal is a crystalline powder melting at 76°, and is sparingly soluble in water and in alcohol.

CHAPTER XVIII

THE ETHERS

THE ethers are compounds whose molecules consist of an oxygen atom to which two alkyl radicles are attached. Theoretically, they may be regarded as the oxides of the alkyl radicles, the alcohols being the hydroxides. Thus we have :

$CH_3.OH$	$(CH_3)_2O$
Methyl alcohol.	Dimethyl ether.

with which compare :

$Na.OH$	Na_2O
Sodium hydroxide.	Sodium oxide.

The two alkyl radicles in an ether may be the same or In the former case the compound is called a simple ethe the latter case a mixed ether.

The ethers form a homologous series, of which the fc members are :

Dimethyl ether, $CH_3.O.CH_3$,
Methyl ethyl ether, $CH_3.O.C_2H_5$,
Methyl propyl ether, $CH_3.O.C_3H_7$,
Diethyl ether, $C_2H_5.O.C_2H_5$.

The only ether of any great importance is diethyl ether, usually known as " ether ".

DIETHYL ETHER. ETHER $(C_2H_5)_2O$

Preparation.—(1) Ether can be prepared by heating an ethyl halide with dry sodium ethoxide :

$$C_2H_5Br + C_2H_5.ONa = C_2H_5.O.C_2H_5 + NaBr.$$

This is a general method for the preparation of compounds of the ether type. It is particularly applicable to the preparation of mixed ethers. Methyl ethyl ether, for example, can be prepared by heating an ethyl halide with sodium methoxide :

$$C_2H_5I + CH_3.ONa = C_2H_5.O.CH_3 + NaI.$$

(2) In the laboratory, it is prepared by heating a mixture of ethyl alcohol and concentrated sulphuric acid.

The apparatus (Fig. 6) consists of a half-litre distillation flask, connected by means of a cork to a long Liebig's condenser. The other end of the condenser is attached to an adapter, and the receiver (a 250-mil flask or bottle) is surrounded with broken ice. The distillation flask is provided with a double-bored cork, through the holes of which pass a thermometer and a dropping funnel.[1]

A mixture of concentrated sulphuric acid (54 mils) and absolute alcohol (68 mils) is prepared by slowly running the acid into the alcohol, with constant shaking and cooling under the tap if necessary.

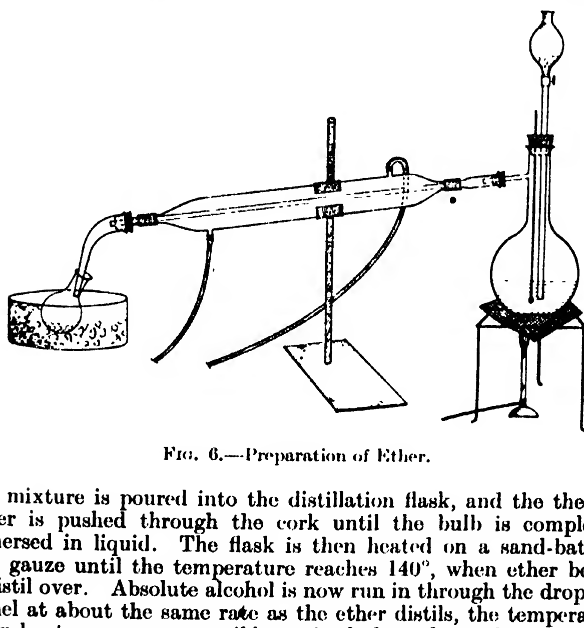


FIG. 6.—Preparation of Ether.

The mixture is poured into the distillation flask, and the thermometer is pushed through the cork until the bulb is completely immersed in liquid. The flask is then heated on a sand-bath or wire gauze until the temperature reaches 140°, when ether begins to distil over. Absolute alcohol is now run in through the dropping funnel at about the same rate as the ether distils, the temperature being kept as near as possible to 140° throughout the operation. The process can be continued until about 80 mils of alcohol have been added through the funnel.

The ether obtained in this way contains water, alcohol, and sulphurous acid (formed by reduction of some of the sulphuric

[1] In carrying out this preparation, special precautions must be taken against the possibility of the ether vapour taking fire. All corks should be a tight fit, a good stream of water should be maintained through the condenser, and it is advisable to interpose some simple form of screen, such as a large sheet of cardboard, between the distillation flask and the receiver.

acid), from which it must be freed. It is therefore washed by shaking it in a separating funnel with a small quantity of dilute sodium hydroxide solution, allowing to separate, and running off the lower aqueous layer. The washing is repeated, and the ether is then dried by adding small lumps of anhydrous calcium chloride, and allowing it to stand, loosely corked, for at least half an hour. The ether is finally decanted from the calcium chloride into a dry flask, and distilled from a water-bath.

Ether prepared in this way is tolerably pure and dry. It can be freed from the last traces of water and alcohol by allowing it to stand for twenty-four hours over pieces of metallic sodium, in a flask closed by a cork through which a calcium chloride tube passes, and then distilling it from the sodium residues.

The formation of ether by this method is explained as follows. On mixing the alcohol with the concentrated sulphuric acid, ethyl hydrogen sulphate is formed:

$$C_2H_5.OH + H_2SO_4 = C_2H_5.HSO_4 + H_2O.$$

This compound, on heating with alcohol, yields ether and sulphuric acid:

$$C_2H_5.HSO_4 + C_2H_5.OH = C_2H_5.O.C_2H_5 + H_2SO_4.$$

None of the sulphuric acid is used up during these reactions, so that a given quantity of the acid is able to convert a relatively large quantity of alcohol into ether. However, side reactions cause some of the acid to be reduced to sulphur dioxide, and after a time the acid becomes so diluted by the water produced that the process has to be discontinued.

This preparation should be carefully compared with that of ethylene (p. 210). Both reactions take place in two stages, and the first product in each case is ethyl hydrogen sulphate. If a large excess of sulphuric acid is used and the mixture is heated to a high temperature, the ethyl hydrogen sulphate is decomposed, with formation of ethylene; if, on the other hand, a comparatively large proportion of alcohol is used and the temperature is kept lower, ether is the main product.

Properties.—Ether is a colourless, very mobile liquid, with a characteristic odour. Its specific gravity is 0·74, and it boils at 35°. It is miscible with alcohol in all proportions, but is only soluble in water to the extent of about 1 part in 10. The vapour is exceedingly inflammable, and forms an explosive mixture with air. Care should be taken not to handle large quantities of ether anywhere near a naked flame.

In chemical properties ether is a very inert substance. It is not acted upon by metallic sodium or potassium. It is only very slowly attacked by ordinary oxidising agents, and phosphorus pentachloride has no action on it in the cold. Hot concentrated acids decompose ether, with formation of esters. For example:

$$(C_2H_5)_2O + 2HI = 2C_2H_5I + H_2O.$$

That ether must have the constitutional formula assigned to it is obvious from the first method described for its preparation. Its chemical inertness, when compared with the alcohols, is attributable to the absence from the molecule of the very reactive —OH group.

Æther. *Ether.*—The official substance boils from 34-36°, and has a specific gravity of 0·720.

Test for Impurity.—On being allowed to evaporate in a glass dish at ordinary temperatures, it should leave a film of moisture which does not bleach or redden litmus (absence of sulphurous and other acids).

Other common impurities, not mentioned in the Pharmacopœia, are water, alcohol, extractive matter, and—in the case of ether prepared from methylated spirit—methyl compounds.

Æther Purificatus. *Purified Ether.*—This is a specially purified variety of ether, and is described in the Pharmacopœia in addition to Æther. It can be prepared from Æther by further washing and drying, followed by fractional distillation. Æther Purificatus is intended for use as an anæsthetic, and is required to be freer from aldehydes, peroxides, and methyl compounds than is Æther.

CHAPTER XIX

ALDEHYDES AND KETONES

ALDEHYDES and ketones have already been mentioned as oxidation products of primary and of secondary alcohols respectively.

ALDEHYDES

The first two members of the aldehyde series are formaldehyde, $H.CHO$, and acetaldehyde, $CH_3.CHO$, formed by oxidation of methyl and ethyl alcohols respectively. With these two exceptions, the names of aldehydes are derived from those of the corresponding alcohols. Thus the next two members of the series are :

$$\underset{\text{Propaldehyde.}}{CH_3.CH_2.CHO} \text{ derived from } \underset{\text{Normal propyl alcohol.}}{CH_3.CH_2.CH_2.OH.}$$

$$\underset{\text{Normal butaldehyde.}}{CH_3.CH_2.CH_2.CHO} \text{ derived from } \underset{\text{Normal butyl alcohol.}}{CH_3.CH_2.CH_2.CH_2.OH.}$$

FORMALDEHYDE, H.CHO

Preparation.—Formaldehyde is prepared by the atmospheric oxidation of methyl alcohol, metallic copper being used as a catalyst :

$$CH_3.OH + O = H.CHO + H_2O.$$

A stream of air, saturated with the vapour from warm methyl alcohol, is led through a piece of combustion tubing about twelve inches long, containing a roll of bright copper gauze, and attached to a condenser and receiver. The combustion tube is heated until the gauze begins to glow, after which it will continue to do so without further application of heat. The liquid which collects in the receiver consists of formaldehyde, methyl alcohol, and water.

Instead of copper, platinum may be used as a catalyst. This is readily demonstrated by holding a red-hot spiral of platinum wire over some warm methyl alcohol contained in a beaker. The wire continues to glow, and the pungent odour of formaldehyde can be detected.

Properties.—Formaldehyde is a colourless gas having an exceed-

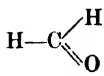
ingly characteristic and irritating odour. It can be condensed to a liquid at $-21°$.

Formaldehyde is a powerful reducing agent, being readily oxidised to formic acid :

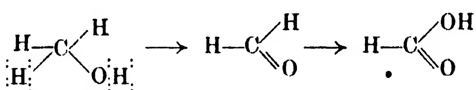
$$H.CHO + O = H.COOH.$$

If a few drops of the aqueous solution are added to some ammoniacal silver nitrate in a test tube, a silver mirror forms on the sides of the tube on standing.

From considerations of valency, the only possible constitutional formula for formaldehyde is



which is usually contracted to H.CHO. This formula shows clearly the relationship of formaldehyde to methyl alcohol on the one hand and to formic acid on the other :



Methyl alcohol. Formaldehyde. Formic acid.

Formalin is a 40 per cent solution of the gas in water, and is the form in which formaldehyde is generally met with in commerce. It is neutral to indicators, possesses the characteristic pungent odour of the gas, and is widely employed as an antiseptic and disinfectant.

Tests for Formaldehyde.—(1) On evaporation, aqueous solutions of formaldehyde leave a solid residue of paraformaldehyde, which sublimes on strongly heating.

(2) Add to silver nitrate solution very dilute ammonium hydroxide until the brown precipitate at first formed just redissolves, then add a few drops of formaldehyde solution, and warm. Metallic silver is deposited, either in the form of a mirror or as a black precipitate.

(3) Add two or three drops of formaldehyde solution to a solution of about 0·1 gramme of salicylic acid in 5 mils of concentrated sulphuric acid. A deep red coloration is produced.

LIQUOR FORMALDEHYDI

Solution of Formaldehyde

The official solution of formaldehyde is required to contain 36-38 grammes of formaldehyde in 100 mils. Its specific gravity lies between 1·079 and 1·081. It may be neutral or slightly acid to litmus.

Tests for Impurities.—To be applied to a 1-5 dilution of the liquor.

Lead.—Add an equal volume of alcohol and a few drops of dilute sulphuric acid. There should be no turbidity.

Copper.—Add excess of ammonium hydroxide, and filter. The filtrate should have no blue tinge, and should not acquire a brown colour on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—Add excess of dilute nitric acid, boil well, and add potassium ferrocyanide, when there should be no blue or green coloration.

Calcium.—Add ammonium hydroxide and ammonium oxalate, when there should be no precipitate.

Chloride.—Acidify with nitric acid and add silver nitrate. There should be no opalescence.

Sulphate.—Acidify with hydrochloric acid and add barium chloride. There should be no turbidity.

Acetone.—To 5 mils of the diluted solution add about 10 mils of N/10 iodine, nearly decolorise the mixture with sodium hydroxide, and warm. No yellow crystalline precipitate of iodoform should be produced.

Quantitative Estimation.—The estimation of this solution depends upon its oxidation to formic acid in the presence of standard alkali, the excess of alkali being determined by titration with standard acid.

3 mils of the solution, measured from a burette, are added to 50 mils of N/1 sodium hydroxide solution in a 250-mils conical flask. About 50 mils of solution of hydrogen peroxide (10-volume strength) is added, and the mixture is heated on a water-bath until all evolution of oxygen has ceased. A few drops of phenolphthalein is then added, and the solution is titrated with N/1 sulphuric acid.

Since the solution of hydrogen peroxide may contain free acid, a blank experiment is performed without the addition of the formaldehyde solution. The volume of N/1 acid required in the blank experiment may be taken as equivalent to the effective volume of alkali employed in the estimation proper. The volume of N/1 acid required in the estimation, subtracted from this volume of effective alkali, gives the volume of alkali used in neutralising the formic acid :

$$H.CHO + O = H.COOH,$$
$$H.COOH + NaOH = H.COONa + H_2O,$$
$$NaOH \equiv H.CHO,$$
$$40 \equiv 30,$$
$$1000 \text{ mils of N/1 NaOH} \equiv 30 \text{ grammes of H.CHO},$$
$$1 \text{ mil of N/1 NaOH} \equiv 0{\cdot}030 \text{ gramme of H.CHO}.$$

Derivatives of Formaldehyde

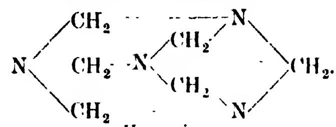
Polymers of Formaldehyde.—Two or more molecules of formaldehyde can be readily induced to combine together, forming compounds

whose molecular formulæ are simple multiples of that of the parent substance. Such compounds are known as polymers or polymerides.

When a solution of formaldehyde is evaporated to dryness, a white amorphous solid remains. This solid is formed by polymerisation of some of the formaldehyde, and consists of *paraformaldehyde*, $(CH_2O)_2$.

Metaformaldehyde, trioxymethylene, $(CH_2O)_3$, is a crystalline solid, and is slowly formed by spontaneous polymerisation of liquid formaldehyde.

Hexamina. *Hexamine.* *Syn.* Hexamethylenetetramine.—This is a complex compound of the following constitution :



Hexamine.

It is prepared by mixing aqueous solutions of formaldehyde and ammonium hydroxide, and evaporating to dryness on a water-bath :

$$6CH_2O + 4NH_3 = C_6H_{12}N_4 + 6H_2O.$$

Hexamine is a colourless, crystalline powder, readily soluble in water, but somewhat less soluble in alcohol. When heated, it sublimes at 263° without melting. It is easily hydrolysed by boiling dilute acids yielding formaldehyde and an ammonium salt.

Hexamine is commonly known as " urotropine ".

Quantitative Estimation. — Hexamine is estimated by hydrolysing with standard acid, when the ammonia which is produced neutralises an equivalent amount of the acid. The excess of acid is then determined by titration with standard alkali. Weigh 1 gramme, mix with 35 mils of N/1 sulphuric acid, evaporate on a water-bath until the odour of formaldehyde has disappeared, and then titrate with N/1 sodium hydroxide, using methyl orange as indicator :

$$C_6H_{12}N_4 + 6H_2O + 2H_2SO_4 = 6H.CHO + 2(NH_4)_2SO_4,$$
$$2H_2SO_4 \equiv C_6H_{12}N_4,$$
$$2 \times 98 \equiv 140,$$
$$1000 \text{ mils N/1 } H_2SO_4 \equiv 35 \text{ grammes of } C_6H_{12}N_4,$$
$$1 \text{ mil N/1 } H_2SO_4 \equiv 0{\cdot}035 \text{ gramme of } C_6H_{12}N_4.$$

Hexamine is required to contain not less than 98 per cent of $C_6H_{12}N_4$.

ACETALDEHYDE, $CH_3.CHO$

Preparation.—(1) Acetaldehyde can be made by strongly heating a dry mixture of calcium formate and calcium acetate :

$$\underset{\text{Calcium formate.}}{(H.COO)_2Ca} + \underset{\text{Calcium acetate.}}{(CH_3.COO)_2Ca} = 2CH_3.CHO + 2CaCO_3.$$

(2) In the laboratory it is prepared by the oxidation of ethyl alcohol:

$$CH_3.CH_2.OH + O = CH_3.CHO + H_2O.$$

A solution of potassium dichromate is warmed in a distillation flask attached to an efficient condenser, and a mixture of alcohol and sulphuric acid is slowly run in through a dropping funnel. Considerable heat is evolved, and acetaldehyde, together with some water and alcohol, distils. On account of the low boiling-point of the aldehyde, the receiver must be cooled in ice. The distillate is purified by fractional distillation from a water-bath.

Properties.—Acetaldehyde, often simply called aldehyde, is a colourless, mobile liquid, of specific gravity 0·8 and boiling-point 21°. It has a characteristic, penetrating, but not unpleasant odour, and is miscible with water, alcohol, and ether.

Like formaldehyde, it is a powerful reducing agent. Thus it precipitates silver from ammoniacal silver nitrate, being itself oxidised to acetic acid:

$$CH_3.CHO + O = CH_3.COOH.$$

Nascent hydrogen reduces it to ethyl alcohol:

$$CH_3.CHO + 2\hat{H} = CH_3.CH_2.OH.$$

It is readily acted upon by phosphorus pentachloride, PCl_5, the oxygen atom being displaced by two chlorine atoms:

$$CH_3.CHO + PCl_5 = \underset{\text{Ethylidene dichloride.}}{CH_3.CHCl_2} + POCl_3.$$

Acetaldehyde combines directly with ammonia and with sodium bisulphite, forming additive products:

$$CH_3.CHO \xrightarrow{NH_3} CH_3.CH\begin{matrix}/OH \\ \backslash NH_2\end{matrix}$$

Acetaldehyde ammonia.

$$CH_3.CHO \xrightarrow{NaHSO_3} CH_3.CH\begin{matrix}/OH \\ \backslash SO_3Na.\end{matrix}$$

Acetaldehyde sodium bisulphite.

These additive products are both colourless, crystalline substances, and are decomposed by boiling dilute acids or alkalies with regeneration of the aldehyde.

Acetaldehyde also combines directly with hydrocyanic acid (p. 300) to form a compound called a *cyanohydrin*:

$$CH_3.CHO + HCN \longrightarrow CH_3.CH\begin{matrix}\diagup OH\\ \diagdown CN.\end{matrix}$$

Acetaldehyde cyanohydrin.

Acetaldehyde reacts readily with hydroxylamine, NH_2OH, and with phenyl hydrazine, $C_6H_5.NH.NH_2$ (p. 344). In both reactions a molecule of water is eliminated, the product in the first case being an *oxime*, and in the second a *phenylhydrazone*:

$$CH_3.CHO + NH_2OH = CH_3.CH:N.OH + H_2O,$$

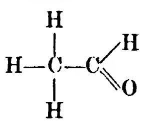
Acetaldoxime.

$$CH_3.CHO + C_6H_5.NH.NH_2 = CH_3.CH:N.NH.C_6H_5 + H_2O.$$

Acetaldehyde phenylhydrazone.

When warmed with a strong solution of sodium or potassium hydroxide, acetaldehyde is converted into a complex brown resin—*aldehyde resin*.

Constitution.—By analogy with formaldehyde, the constitutional formula of acetaldehyde may be written

 or $CH_3.CHO$,

which is in agreement with its formation from ethyl alcohol and its conversion into acetic acid on oxidation:

$$CH_3.CH_2.OH \longrightarrow CH_3.CHO \longrightarrow CH_3.COOH.$$

Amongst the more important points in support of this formula are:

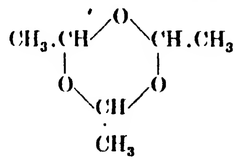
(i.) By the action of phosphorus pentachloride the oxygen atom of acetaldehyde is displaced by two atoms of chlorine, showing that this oxygen atom was probably joined to a carbon atom by a double bond. This reaction should be contrasted with the action of phosphorus pentachloride on compounds containing an —OH group (pp. 218, 247).

(ii.) Acetaldehyde is not "unsaturated" in the same sense as, for example, ethylene. It does not combine directly with halogens or halogen acids—a typical property of compounds containing a double bond between two carbon atoms. It can, however, form additive products under certain conditions; thus, it can combine directly with nascent hydrogen, ammonia, sodium bisulphite, and hydrocyanic acid. These facts are readily explicable on the assumption that the molecule contains a double bond between a carbon and an oxygen atom.

The higher members of the aldehyde series are all very similar

in chemical properties to acetaldehyde, since their reactions are mainly dependent upon the presence in the molecule of the —CHO group.

Paraldehydum, *Paraldehyde* $(C_2H_4O)_3$, is a polymer of acetaldehyde, of the formula



It is easily prepared by adding a drop of concentrated sulphuric acid to acetaldehyde, a vigorous reaction taking place immediately.

It is a colourless liquid, of specific gravity 1·00, and boiling-point 123-125°, has a pleasant, characteristic ethereal odour and a cool, acrid taste, and is neutral to litmus. It is soluble 1-9 in water, and miscible with alcohol and ether, and has the unusual property of being less soluble in hot water than in cold.

When paraldehyde is distilled with a little concentrated sulphuric acid, it is reconverted into acetaldehyde.

CHLORAL, $CCl_3.CHO$

This important compound may be regarded as derived from acetaldehyde by the substitution of three chlorine atoms for the hydrogen atoms of the methyl group, whence its systematic name — *trichloracetaldehyde.*

Preparation.—Chloral is manufactured by passing chlorine through alcohol, at first in the cold, and finally at about 60°, the whole process occupying some two weeks. The chlorine acts both as an oxidising and a chlorinating agent:

$$CH_3.CH_2.OH + Cl_2 = CH_3.CHO + 2HCl,$$
$$CH_3.CHO + 3Cl_2 = CCl_3.CHO + 3HCl.$$

The chloral, as fast as it is formed, combines with some of the remaining alcohol to form a crystalline additive compound, chloral alcoholate, $CCl_3.CH\begin{cases}OH\\O.C_2H_5.\end{cases}$ This compound is collected and distilled with concentrated sulphuric acid, when chloral passes over. The distillate may be purified by conversion into chloral hydrate (*q.v.*), which is then recrystallised several times from water, and finally distilled with concentrated sulphuric acid to yield pure chloral.[1]

[1] Chloral is also formed, together with other products, by the chlorination of aqueous solutions of acetaldehyde. This is of interest as showing the relationship between chloral and acetaldehyde (see p. 201).

Properties.—Chloral is a colourless, oily liquid with a penetrating odour. Specific gravity, 1·5; boiling-point, 97°.

In many of its chemical properties chloral resembles acetaldehyde. It reduces ammoniacal silver nitrate, being itself oxidised to trichloracetic acid (p. 247):

$$CCl_3.CHO + O = CCl_3.COOH.$$

It combines with ammonia and with sodium bisulphite to form additive compounds, and polymerises when treated with acids.

When warmed with a solution of sodium or potassium hydroxide, chloral yields chloroform:

$$CCl_3.CHO + KOH = CHCl_3 + \underset{\text{Potassium formate.}}{H.COOK.}$$

CHLORAL HYDRAS

Chloral Hydrate, $CCl_3.CH(OH)_2$

Preparation.—If a little water is added to chloral, the mixture solidifies, with evolution of heat, owing to the formation of the hydrate:

$$CCl_3.CHO + H_2O \longrightarrow CCl_3.CH\begin{cases}OH \\ OH.\end{cases}$$

The product can be purified by recrystallisation from water.

Properties.—Colourless, crystalline plates, which melt at 49-53°, and have a characteristic odour. Soluble more than 1-1 in water, alcohol, or ether, and 1-3 in chloroform.

If chloral hydrate is distilled with concentrated sulphuric acid, it yields chloral as the distillate.

Tests for Impurities. *Free Acids.*—Chloral hydrate should be neutral or only slightly acid to litmus.

Non-volatile Solids.—At a temperature slightly above its melting-point it should volatilise, leaving no residue.

Readily Carbonisable Organic Impurities.—A solution in chloroform, shaken with concentrated sulphuric acid, should impart no colour to the acid.

Chloral Alcoholate.—Warm about 1 gramme with 6 mils of 2 per cent sodium hydroxide solution, in order to decompose any alcoholate present. Filter, and test for alcohol in the filtrate by adding sufficient iodine solution to impart a deep brown colour, and setting aside for an hour. No precipitate of iodoform should be produced.

Chloride.—Test the aqueous solution with silver nitrate, when there should be no precipitate.

Chloral Formamidum. *Chloral Formamide. Syn.* Chloral-amide, $CCl_3.CH(OH).NH.CHO$.—This is prepared by the direct combination of chloral and formamide (p. 246):

$$CCl_3.CHO + H.CO.NH_2 = CCl_3.CH\begin{cases}OH\\NH.CHO.\end{cases}$$

Butyl-Chloral Hydras, *Butyl-Chloral Hydrate*, $CH_3.CHCl.CCl_2.CH(OH)_2$.—The parent substance, butyl chloral, $CH_3.CHCl.CCl_2.CHO$, is prepared by the prolonged action of chlorine on acetaldehyde. The reaction is complex, and probably takes place in the following stages:

$$CH_3.CHO + Cl_2 = CH_2Cl.CHO + HCl,$$
$$CH_3.CHO + CH_2Cl.CHO = CH_3.CH:CCl.CHO + H_2O,$$
$$CH_3.CH:CCl.CHO + Cl_2 = CH_3.CHCl.CCl_2.CHO.$$

Butyl chloral is an oil boiling at 164°, and from it the hydrate is prepared by addition of water.

Butyl-chloral hydrate forms colourless, pearly-white crystals, melting at 78°, and has a pungent odour. It is sparingly soluble in water, readily in alcohol, forming neutral solutions.

KETONES

Ketones are formed by oxidation of secondary alcohols (p. 225), and resemble aldehydes in containing the carbonyl group, $>C=O$, only in this case the group is attached to two alkyl radicles. Ketones are, in general, named according to the alkyl radicles in the molecule; for example:

$$\begin{matrix}CH_3\\C_2H_5\end{matrix}\!\!>CO \qquad\qquad \begin{matrix}C_2H_5\\C_2H_5\end{matrix}\!\!>CO$$

Methyl ethyl ketone. Diethyl ketone.

It is only necessary to describe in detail one ketone, namely, dimethyl ketone or acetone, which is the lowest and most important member of the series. The higher ketones closely resemble acetone in chemical properties, and can be prepared by similar methods.

ACETONE, DIMETHYLKETONE, $CH_3.CO.CH_3$

Preparation.—(1) Acetone can be made by oxidising isopropyl alcohol with chromic acid:

$$(CH_3)_2CH.OH + O = (CH_3)_2CO + H_2O.$$

(2) A more convenient method is by heating calcium or barium acetate in a flask or tube of hard glass : [1]

$$(CH_3.COO)_2Ca = (CH_3)_2CO + CaCO_3.$$

The condensed vapours are redistilled from a water-bath, and the impure acetone thus obtained is shaken with a strong solution of sodium bisulphite. The crystals of acetone sodium bisulphite which separate are filtered off, freed from mother liquor, and distilled with a solution of sodium carbonate. The distillate, which consists of pure aqueous acetone, is dried over calcium chloride and distilled.

(3) Acetone is one of the products of the destructive distillation of wood. The liquor remaining after separating the methyl alcohol as its calcium chloride compound (p. 216) is an aqueous solution of crude acetone, from which pure acetone can be isolated by a method similar to that described above.

Properties.—Acetone is a colourless, mobile, volatile liquid, with a peculiar tarry odour. Its specific gravity is 0·795, it boils at 56-57°, and is miscible with water, alcohol, and ether.

In chemical properties acetone *resembles* the aldehydes in the following respects :

It is readily reduced by nascent hydrogen, yielding the corresponding alcohol :

$$(CH_3)_2CO + 2H = (CH_3)_2CH.OH$$

Isopropyl alcohol.

It combines directly with sodium bisulphite and with hydrocyanic acid :

$$(CH_3)_2CO + NaHSO_3 \longrightarrow (CH_3)_2C\begin{cases} OH \\ SO_3Na \end{cases}$$

Acetone sodium bisulphite.

$$(CH_3)_2CO + HCN \longrightarrow (CH_3)_2C\begin{cases} OH \\ CN \end{cases}$$

Acetone cyanohydrin.

It reacts with hydroxylamine and with phenyl hydrazine, giving an oxime and a phenylhydrazone respectively :

$$(CH_3)_2CO + NH_2OH = (CH_3)_2C : N.OH + H_2O$$

Dimethyl ketoxime.

$$(CH_3)_2CO + C_6H_5.NH.NH_2 = (CH_3)_2C : N.NH.C_6H_5 + H_2O$$

Acetone phenylhydrazone.

[1] It is important to notice that the calcium salts of acetic and higher fatty acids (p. 243) if heated alone yield ketones, but when heated with calcium formate they yield aldehydes.

Acetone *differs* from aldehydes in the following respects :

It is not a reducing agent, and can only be oxidised with difficulty, the molecule being broken up.
It does not combine with ammonia.
It does not resinify when warmed with sodium or potassium hydroxide.
It does not polymerise.

In the presence of certain dehydrating agents, two or more molecules of acetone combine with elimination of water. Thus, when acetone is distilled with fairly concentrated sulphuric acid, it is converted into the hydrocarbon mesitylene (p. 331) :

$$3(CH_3)_2CO = \underset{\text{Mesitylene.}}{C_6H_3(CH_3)_3} + 3H_2O.$$

Changes of this type, in which two or more molecules become joined together with elimination of water, are known as *condensation* reactions. Condensation must be carefully distinguished from polymerisation, in which no water is eliminated.

Tests for Acetone.—(1) It can be recognised by its characteristic odour. The boiling-point affords confirmation of identity, although it is apt to be somewhat variable, except in the case of very pure samples.

(2) Add a few drops to a solution of sodium hydroxide, then add a crystal of iodine, and warm. A yellow precipitate of iodoform is produced, recognisable by its characteristic odour.

(3) Shake well with an equal volume of a cold, nearly saturated solution of sodium bisulphite. A heavy, white, crystalline precipitate of acetone sodium bisulphite separates out.

ACETONUM

Acetone

The official substance has a specific gravity of 0·795-0·798. Not less than 95 per cent should distil between 55 and 57°.

Tests for Impurities. *Solids.*—It should leave no residue when evaporated on a water-bath.

Water (Limit of).—It should yield a clear mixture, with an equal volume of petroleum spirit.

Free Acids (Limit of).—10 mils, to which a few drops of phenolphthalein have been added, should require not more than 10 drops of N/10 sodium hydroxide to produce a permanent pink coloration.

Readily Oxidisable Impurities (Limit of).—20 mils should not completely decolorise 0·1 mil of N/10 potassium permanganate within fifteen minutes.

CHAPTER XX

THE MONOBASIC CARBOXYLIC ACIDS AND THEIR DERIVATIVES

THE FATTY ACIDS

THE so-called " fatty acids " form a homologous series, each memb consisting of an alkyl radicle attached to the " carboxyl " grou

$$-C\begin{matrix}\nearrow OH\\ \searrow O\end{matrix}$$ or —COOH. The fatty acids are the final products of tl oxidation of the primary alcohols, the aldehydes being intermedia products in this process. The names of the acids are generall derived from those of the corresponding aldehydes, the first fi members of the series being :

Formic acid	$H.COOH$.
Acetic acid	$CH_3.COOH$.
Propionic acid	$CH_3.CH_2.COOH$.
Butyric acid	$CH_3.CH_2.CH_2.COOH$.
Iso-butyric acid	$(CH_3)_2CH.COOH$.

The name " fatty acid " was first applied to this series of compound on account of the fact that certain of the higher members, notabl stearic and palmitic acids (p. 252), are important constituents o animal fats.

FORMIC ACID, H.COOH

Formic acid is secreted in considerable quantities by ants, an is also said to occur in nettles and other stinging plants. The aci was formerly obtained by crushing ants with water and distillin the aqueous extract.

Preparation.—(1) Formic acid is produced by the oxidation o methyl alcohol or formaldehyde by atmospheric oxygen in presence of platinum black as catalyst. This provides a method by which formic acid can be synthesised.

$$CH_3.OH \longrightarrow H.CHO \longrightarrow H.COOH.$$

(2) Another synthetic method is by heating potassium hydroxide in an atmosphere of carbon monoxide. In this way potassium

formate is produced, from which the free acid can be liberated by the action of dilute sulphuric acid :

$$\underset{\text{Potassium formate.}}{KOH + CO = H.COOK.}$$

(3) Formic acid is produced when hydrocyanic acid is hydrolysed (by heating it in a sealed tube with a dilute mineral acid) :

$$HCN + 2H_2O + HCl = H.COOH + NH_4Cl.$$

(4) Formic acid is produced, in small quantities, when oxalic acid is heated :

$$\underset{\text{Oxalic acid.}}{(COOH)_2} = H.COOH + CO_2.$$

In the laboratory, formic acid can be conveniently prepared by heating crystalline oxalic acid, with twice its weight of glycerin, at 100°-110°, in a retort to which a Liebig's condenser is attached. An aqueous solution, containing about 50 per cent of formic acid, distils over. When the reaction slackens, a further quantity of formic acid can be obtained by allowing the retort to cool somewhat, introducing a further quantity of oxalic acid, and again heating to 100°-110°.

The reaction takes place in several stages. First, the glycerin, which is a compound of the alcohol type containing three —OH groups, reacts with some of the oxalic acid to form an ester—glyceryl mono-oxalate, or monoxalin. At the temperature employed this ester decomposes into carbon dioxide and glyceryl monoformate, or monoformin. The monoformin then reacts with more oxalic acid to produce monoxalin and formic acid :

$$\begin{array}{lclcll}
CH_2.OH & & COOH & & CH_2.O.CO.COOH & \\
| & + & | & & | & \\
CH.OH & & COOH & \longrightarrow & CH.OH & + H_2O. \\
| & & & & | & \\
CH_2.OH & & & & CH_2.OH & \\
\text{Glycerin} & & \text{Oxalic acid.} & & \text{Monoxalin.} &
\end{array}$$

$$\begin{array}{lcll}
CH_2.O.CO.COOH & & CH_2.O.CHO & \\
| & & | & \\
CH.OH & \longrightarrow & CH.OH & + CO_2. \\
| & & | & \\
CH_2.OH & & CH_2.OH & \\
\text{Monoxalin.} & & \text{Monoformin.} &
\end{array}$$

$$\begin{array}{lclcll}
CH_2.O.CHO & & COOH & & CH_2.O.CO.COOH & \\
| & + & | & & | & \\
CH.OH & & COOH & \longrightarrow & CH.OH & + H.COOH. \\
| & & & & | & \\
CH_2.OH & & & & CH_2.OH & \\
\text{Monoformin.} & & \text{Oxalic acid.} & & \text{Monoxalin.} & \text{Formic acid.}
\end{array}$$

The last two reactions then proceed in a continuous cycle, so that a small quantity of glycerin can bring about the conversion of a relatively large quantity of oxalic acid into formic acid.

The aqueous formic acid obtained in this way is treated with excess of litharge, heated to boiling, and filtered. The filtrate is concentrated and allowed to cool, when lead formate is deposited in colourless crystals :

$$2H.COOH + PbO = (H.COO)_2Pb + H_2O.$$

The crystals are collected, dried, and heated in a current of hydrogen sulphide, when anhydrous formic acid is obtained :

$$(H.COO)_2Pb + H_2S = 2H.COOH + PbS.$$

Properties.—Formic acid is a colourless liquid with a very pungent odour resembling that of sulphur dioxide. Its specific gravity is 1·22, and it boils at 101°. If allowed to come into contact with the skin it causes blisters.

Formic acid turns blue litmus red, and dissolves metallic oxides and carbonates with formation of salts (the formates), and in this way it resembles a weak mineral acid.

Unlike any other member of the fatty acid series, formic acid is a powerful reducing agent, being readily oxidised to carbon dioxide and water :

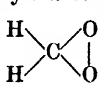
$$H.COOH + O = H_2O + CO_2.$$

Thus it reduces ammoniacal silver nitrate on warming, with formation of a silver mirror. This peculiar behaviour is due to the fact that its molecule still contains the aldehyde group, —CHO.

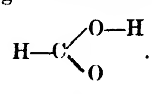
Formic acid is decomposed by warm concentrated sulphuric acid into carbon monoxide and water :

$$H.COOH = CO + H_2O.$$

Constitution.—From considerations of valency, formic acid must be represented by one of the following constitutional formulæ :



(I.)



(II.)

Now formic acid is a monobasic acid, since only one of its hydrogen atoms can be displaced by a metal. This shows that the two hydrogen atoms are in different states of combination. Further, it is a powerful reducing agent, and probably contains the aldehyde group, —CHO. Both these facts point to Formula II. as being correct, and this is generally accepted.

Salts of Formic Acid.—The formates are prepared by the action of the acid on metallic carbonates, oxides, or hydroxides, the metal displacing the hydrogen of the —OH group. Most of them are readily soluble in water ; sodium formate, H.COONa, and potassium

formate, H.COOK, are deliquescent. Ammonium formate, on heating, yields formamide, a compound used in the preparation of Chloral Formamidum (p. 240):

$$\underset{\text{Ammonium formate.}}{H.COONH_4} = \underset{\text{Formamide.}}{H.CO.NH_2} + H_2O.$$

ACETIC ACID, $CH_3.COOH$

Preparation.—(1) Acetic acid can be made by oxidising ethyl alcohol or acetaldehyde by means of air or oxygen, in the presence of platinum black as a catalyst:

$$CH_3.CH_2.OH + O = CH_3.CHO + H_2O,$$
$$CH_3.CHO + O = CH_3.COOH.$$

The oxidation can also be brought about by a living organism, *Mycoderma aceti*, which is present in the atmosphere, and on this fact depends the preparation of vinegar from alcoholic liquors.

Malt vinegar is a brownish liquid containing about 5 per cent of acetic acid. It can be prepared by simply exposing beer to the air for several days, but in practice a little of the organism, in the form of "mother of vinegar", is added to accelerate the process. Ordinary vinegar is mostly prepared from poor French or German wines by exposing to air in vats in the presence of the organism.

(2) Potassium acetate is formed when potassium methoxide is heated in an atmosphere of carbon monoxide:

$$CH_3.OK + CO = CH_3.COOK.$$

(3) Acetic acid is formed when methyl cyanide is hydrolysed by boiling with a dilute mineral acid:

$$\underset{\text{Methyl cyanide.}}{CH_3.CN} + 2H_2O + HCl = CH_3.COOH + NH_4Cl.$$

This is an example of an important general reaction, since all alkyl cyanides, on hydrolysis, are converted into the corresponding carboxylic acids.

(4) Acetic acid is manufactured from the "pyroligneous acid" obtained by the destructive distillation of wood. The "fixing" of the acetic acid by milk of lime has already been described (p. 216). The liquid is separated from tarry matter, evaporated to dryness, and the dry calcium acetate thus obtained is distilled with concentrated sulphuric acid:

$$(CH_3.COO)_2Ca + H_2SO_4 = 2CH_3.COOH + CaSO_4.$$

The distillate is a strong solution of fairly pure acetic acid. The pure anhydrous acid, "glacial" acetic acid, is obtained from this by neutralising with sodium carbonate, crystallising out the sodium

acetate formed, heating to expel water of crystallisation, and distilling with concentrated sulphuric acid.

Properties.—When absolutely pure and free from water, acetic acid is a colourless, crystalline solid, melting at 16·5°, and boiling at 118°. The crystals are very hygroscopic, and liquefy on exposure to moist air. The acid has a sour taste and a very pungent odour, and blisters the skin. It mixes with water and alcohol in all proportions.

In chemical properties acetic acid behaves like a weak mineral acid. It is acid to litmus and to phenolphthalein, and reacts with metallic oxides, hydroxides, and carbonates with formation of salts, but, unlike formic acid, it has no reducing properties.

When chlorine is passed into boiling acetic acid a mixture of the following three compounds is produced, the proportion of each depending upon the duration of the " chlorination " :

Mono-chloracetic acid . . .	$CH_2Cl.COOH$.
Di-chloracetic acid . . .	$CHCl_2.COOH$.
Tri-chloracetic acid . . .	$CCl_3.COOH$.

The chloracetic acids are strong acids. The mono- and tri- compounds are solids, but the di- is a liquid. Tri-chloracetic acid is usually made by oxidising chloral (p. 238).

Constitution.—The formation of acetic acid from ethyl alcohol is apparently analogous to the preparation of formic acid from methyl alcohol. This suggests that acetic acid has the formula $CH_3.C\begin{smallmatrix}\diagup OH\\ \diagdown O\end{smallmatrix}$, as will be seen if the two reactions are written in the following way :

$$H.CH_2.OH \longrightarrow H.COOH,$$
$$CH_3.CH_2.OH \longrightarrow CH_3.COOH.$$

The same conclusion is arrived at if we compare the formation of formic acid from hydrocyanic acid with that of acetic acid from methyl cyanide :

$$H.CN \longrightarrow H.COOH,$$
$$CH_3.CN \longrightarrow CH_3.COOH.$$

The chemical properties of acetic acid confirm these views, and the following facts may be mentioned in support of the accepted constitutional formula :

(i.) Acetic acid is monobasic. Only one of its hydrogen atoms can be displaced by a metal, showing that this hydrogen atom is in a different state of combination from the other three.

(ii.) By the action of phosphorus pentachloride on acetic acid (p. 250) the oxygen atom and one hydrogen atom are together displaced by *one* atom of chlorine, thus showing that the molecule contains the univalent —OH group (compare p. 218).

(iii.) Three hydrogen atoms of acetic acid can be successively

displaced by chlorine atoms by the direct action of chlorine gas, with formation of mono-, di-, and tri-chloracetic acids. This suggests that these three hydrogen atoms are directly attached to carbon, as in the case of the hydrogen atoms of methane.

Salts of Acetic Acid.—The acetates are crystalline solids, most of them being readily soluble in water. Potassium acetate, $CH_3.COOK$, is deliquescent. Ammonium acetate yields acetamide (p. 251) when it is heated :

$$\underset{\text{Ammonium acetate.}}{CH_3.COONH_4} = \underset{\text{Acetamide.}}{CH_3.CO.NH_2} + H_2O.$$

Sodium and lead acetates both crystallise with three molecules of water. A solution of lead acetate (sugar of lead) reacts with litharge to form lead subacetate (p. 171). Verdigris is a basic acetate of copper, $(CH_3.COO)_2Cu,Cu(OH)_2$.

The following acetates are official, and have been previously described :

Liquor Ammonii Acetatis (p. 95).
Plumbi Acetas, $Pb(C_2H_3O_2)_2,3H_2O$ (p. 170).
Liquor Plumbi Subacetatis Fortis (p. 171).
Potassii Acetas, $KC_2H_3O_2$ (p. 66).
Zinci Acetas, $Zn(C_2H_3O_2)_2,2H_2O$ (p. 119).

Tests for Acetates.—(1) Heat with dilute or strong sulphuric acid, when the pungent odour of acetic acid will be detected. No charring takes place.

(2) Warm with concentrated sulphuric acid and a little alcohol. Ethyl acetate is formed, which may be recognised by its pleasant, fruity odour.

(3) Add to a neutral solution of an acetate a few drops of ferric chloride solution. The liquid turns deep red, owing to the formation of ferric acetate in solution, and, on boiling, a brown, flocculent precipitate of basic ferric acetate is produced.

ACIDUM ACETICUM

Acetic Acid, $CH_3.COOH$. (Mol. Wt. = 60)

This is required to contain 33 per cent by weight of $CH_3.COOH$ and 67 per cent by weight of water. Specific gravity 1·044.

Tests for Impurities. *Non-volatile Solids.*—It should leave no residue on evaporation.

Copper.—Dilute and add potassium ferrocyanide, when there should be no brown coloration.

Lead.—When tested by the limit test (p. 173), using 10 grammes in each Nessler glass, no difference in colour should be observed on adding the solution of sodium sulphide to one of the solutions.

Sulphate and Sulphite.—Add dilute hydrochloric acid and barium chloride, when there should be no turbidity (absence of sulphate).

Filter, if necessary, and add bromine water to the filtrate, when there should be no further turbidity (absence of sulphite).

Chloride.—Add nitric acid and silver nitrate, when there should be no opalescence.

Nitrate.—Apply the brown ring test (p. 35).

Formate.—Neutralise exactly with ammonium hydroxide, add silver nitrate, and warm. There should be no immediate darkening in colour.

Tarry Matter (Limit of).—To 2 mils add a mixture of 1 drop of 1 per cent potassium permanganate solution and 10 mils of water. The liquid should not be decolorised within half a minute.

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—It is estimated by neutralisation with standard sodium hydroxide. Weigh about 3 grammes in a stoppered weighing bottle, and dilute to 100 mils. Titrate portions of 20 mils with N/10 sodium hydroxide, using phenolphthalein as indicator :

$$NaOH + CH_3.COOH = CH_3.COONa + H_2O,$$
$$40 \equiv 60,$$
$$1000 \text{ mils of N/1 NaOH} \equiv 60 \text{ grammes of } CH_3.COOH,$$
$$1 \text{ mil N/10 NaOH} \equiv 0{\cdot}0060 \text{ gramme of } CH_3.COOH.$$

Acidum Aceticum Dilutum. *Diluted Acetic Acid.*—This contains 5 per cent by weight of acetic acid, and can be made by diluting 152·6 grammes of Acidum Aceticum to 1000 mils with distilled water. Its specific gravity is 1·007.

Tests for Impurities.—It should be free from the impurities mentioned under Acidum Aceticum.

Quantitative Estimation.—Weigh 10 grammes, dilute to 100 mils, and titrate portions of 20 mils with N/10 sodium hydroxide, as described under Acidum Aceticum.

ACIDUM ACETICUM GLACIALE

Glacial Acetic Acid

This is required to contain not less than 98·9 per cent of $CH_3.COOH$.

Properties.—At summer temperatures it is a colourless liquid, but in cold weather it solidifies, partially or completely, to a mass of colourless crystals. It should not completely liquefy again until the temperature rises above 14·7°. It should be noted that the specific gravity is not given in the Pharmacopœia, as this is no criterion of strength. The specific gravity of glacial acetic acid is 1·058. It increases on addition of water until the mixture contains only 77 per cent of acid, reaching at this point a maximum of 1·075. It then begins to decrease with dilution, so that a 46 per cent solution of the acid has the same specific gravity as the glacial. This peculiar behaviour is attributed to the formation of a hydrate, $CH_3.COOH,H_2O$.

Tests for Impurities.—The tests for impurities are as described under Acidum Aceticum, with the following exceptions:

Limit of Tarry Matter.—2 mils should not completely decolorise a mixture of 3 drops of 1 per cent potassium permanganate solution and 10 mils of water within half a minute.

Arsenic.—Should be absent when tested for by Fleitmann's Test (p. 143).

Quantitative Estimation.—Weigh 5 grammes, dilute to 100 mils, and titrate portions of 20 mils with N/1 sodium hydroxide, as described under Acidum Aceticum.

DERIVATIVES OF ACETIC ACID

Most carboxylic acids can be converted into a number of derivatives by changes in which the —COOH group takes part. Thus the —OH can be displaced by a chlorine atom, yielding a compound containing the group —COCl, and called an *acid chloride*; two molecules of the acid can be made to condense together with elimination of a molecule of water, and formation of a compound containing the group $\begin{matrix}\text{—CO}\diagdown \\ \quad\quad \text{O} \\ \text{—CO}\diagup\end{matrix}$ called an *anhydride*; also the acid can be converted into an *amide* containing the group $—CO.NH_2$. Important derivatives of these types can be prepared from acetic acid, and will now be described. They are typical compounds of their respective classes, and their methods of formation and properties are characteristic of those of acid chlorides, anhydrides, and amides in general.

Acetyl chloride, $CH_3.COCl$, is prepared by slowly adding phosphorus tri- or penta-chloride to anhydrous acetic acid:

$$CH_3.COOH + PCl_5 = CH_3.COCl + POCl_3 + HCl.$$

The product is distilled from a water-bath.

Acetyl chloride is a colourless liquid with a very pungent smell, boiling at 55°. It fumes strongly in moist air, and is rapidly decomposed by water, even in the cold, to form acetic and hydrochloric acids:

$$CH_3.COCl + H_2O = CH_3.COOH + HCl.$$

Acetyl chloride reacts with most organic compounds containing the —OH group in a similar way, and it is therefore widely employed for introducing the acetyl group, $CH_3.CO—$, into such compounds; for example:

$$\underset{\text{Propyl alcohol.}}{CH_3.COCl + CH_3.CH_2.CH_2.OH} = \underset{\text{Propyl acetate.}}{CH_3.CO.O.CH_2.CH_2.CH_3} + HCl.$$

Acetic Anhydride, $(CH_3.CO)_2O$.—This compound can be prepared by the action of acetyl chloride on dry sodium acetate:

$$CH_3.COONa + CH_3.COCl = (CH_3.CO)_2O + NaCl.$$

It is a colourless liquid, boiling at 136°, and has a pungent, irritating odour. If added to cold water it sinks to the bottom as a heavy oil, but, on standing, the two liquids slowly react to form acetic acid:

$$(CH_3.CO)_2O + H_2O = 2CH_3.COOH.$$

This reaction takes place rapidly if acetic anhydride is boiled with water.

Acetic anhydride, like acetyl chloride, can be used for introducing the acetyl group into compounds containing the hydroxyl group.

Acetamide, $CH_3.CO.NH_2$, is formed when dry ammonia gas acts on acetyl chloride or acetic anhydride; for example:

$$CH_3.COCl + NH_3 = CH_3.CO.NH_2 + HCl.$$

This is another example of the use of acetyl chloride and acetic anhydride in introducing the acetyl group into compounds.

Acetamide can also be made by shaking ethyl acetate with strong ammonia solution:

$$CH_3.COOC_2H_5 + NH_3 = CH_3.CO.NH_2 + C_2H_5.OH.$$

In the laboratory it is prepared by heating ammonium acetate:

$$CH_3.COONH_4 = CH_3.CO.NH_2 + H_2O.$$

Solid ammonium acetate is distilled from a distillation flask, using as an air condenser a wide glass tube with no water-jacket. That part of the distillate passing over above about 170° solidifies in the receiver, and consists of impure acetamide. It is best purified by fractional distillation.

Acetamide forms small, colourless, needle-like crystals. Melting-point, 82°; boiling-point, 222°. As ordinarily obtained it has a strong smell of mice, but this is due to impurity.

Acetamide is readily hydrolysed by boiling it for some minutes with a solution of an alkali or a dilute mineral acid, acetic acid and ammonia being formed:

$$CH_3.CO.NH_2 + H_2O = CH_3.COOH + NH_3.$$

In the actual process, of course, either the acetic acid or the ammonia is produced in the form of a salt, according to whether an alkali or an acid is used to effect the hydrolysis.

Acetamide loses a molecule of water when heated with phosphorus pentoxide, methyl cyanide being formed:

$$CH_3.CO.NH_2 = CH_3.CN + H_2O.$$

Higher Fatty Acids

Propionic acid, $CH_3.CH_2.COOH$, can be prepared by oxidising propyl alcohol or propaldehyde with acidified potassium dichromate:

$$CH_3.CH_2.CH_2.OH + O = CH_3.CH_2.CHO + H_2O,$$
$$CH_3.CH_2.CHO + O = CH_3.CH_2.COOH.$$

It is a colourless liquid, boiling at 141°. It has a pungent odour, is miscible with water, and closely resembles acetic acid in chemical properties.

Butyric Acids.—There are two acids of the formula $C_3H_7.COOH$, namely:

$CH_3.CH_2.CH_2.COOH$ . . .	Normal butyric acid.
$(CH_3)_2CH.COOH$ . . .	Isobutyric acid.

Normal butyric acid occurs in considerable quantities, combined with glycerin, in butter fat. It can be prepared by adding a little decaying cheese to a dilute solution of a sugar, and keeping the mixture in a warm place. Bacteria present in the cheese bring about the fermentation of the sugar, with formation of butyric acid. During the process the liquid must be kept neutral, or nearly so, by the addition of successive small quantities of calcium carbonate, since the action of the bacteria is inhibited by the presence of much free butyric acid. The butyric acid is thus obtained in the form of its calcium salt, and from this the free acid can be liberated. In modern processes of manufacture pure cultures of butyric acid bacteria are used in place of decaying cheese.

Butyric acid is a sour, viscous liquid, with a very disagreeable odour resembling that of rancid butter, and is miscible with water in all proportions. Some of its esters are pleasant-smelling liquids, and are used as artificial flavourings.

Valerianic Acids.—The acids of the formula $C_4H_9.COOH$, of which there are four, are known as valerianic or valeric acids. By oxidation of commercial amyl alcohol (p. 226) with potassium dichromate and dilute sulphuric acid a product is obtained which consists chiefly of *isovalerianic acid*, together with smaller quantities of *optically active valerianic acid* and other fatty acids:

$$\begin{array}{l} CH_3 \\ CH_3 \end{array}\!\!>CH.CH_2.CH_2.OH \longrightarrow \begin{array}{l} CH_3 \\ CH_3 \end{array}\!\!>CH.CH_2.COOH$$

Iso-amyl alcohol. Isovalerianic acid.

$$\begin{array}{r} CH_3 \\ CH_3.CH_2 \end{array}\!\!>CH.CH_2.OH \longrightarrow \begin{array}{r} CH_3 \\ CH_3.CH_2 \end{array}\!\!>CH.COOH$$

Optically active amyl alcohol. Optically active valerianic acid.

This mixture constitutes commercial isovalerianic acid, and is used in the preparation of zinc valerianate (p 120).

The volatile oil of valerian root and rhizome contains esters which are gradually decomposed, on keeping, by an enzyme present with formation of isovalerianic acid.

Palmitic acid, $C_{15}H_{31}.COOH$, **and stearic acid,** $C_{17}H_{35}.COOH$, are important members of the fatty acid series, and, in combination with glycerin, they form the most important constituents of fats (p. 274). The free acids are colourless, waxy, translucent solids,

melting at 62° and 69° respectively. They are insoluble in water, but readily soluble in alcohol and ether.

It should be noted that the acidic properties of members of the fatty acid series decrease with rise in molecular weight from formic acid upwards. Palmitic and stearic acids, being very high members, are neutral to litmus, and have very feeble acidic properties; they do, however, dissolve in aqueous sodium or potassium hydroxide, with formation of soluble alkali salts or soaps (p. 277).

A mixture of palmitic and stearic acids, obtained from fats, is used in the manufacture of candles.

HYDROXY-MONOCARBOXYLIC ACIDS

These are derived from the fatty acids by displacement of a hydrogen atom of the alkyl radicle by the group —OH. They form a homologous series, of which the first member is glycollic acid, or hydroxy-acetic acid, $CH_2(OH).COOH$.

Two hydroxy-acids may be derived from propionic acid, $CH_3.CH_2.COOH$, according as to which carbon atom of the alkyl group the substituent —OH group is attached. To differentiate between these compounds, the alkyl carbon atoms in propionic acid are distinguished by Greek letters, the lettering commencing with the carbon atom directly attached to the —COOH group.[1] Thus:

$$\overset{\beta}{C}H_3.\overset{\alpha}{C}H_2.COOH.$$

The two hydroxy-propionic acids are: *Lactic acid*, or α-hydroxy-propionic acid, $CH_3.CH(OH).COOH$; *Hydracrylic acid*, or β-hydroxy-propionic acid, $CH_2(OH).CH_2.COOH$. Of these, lactic acid is by far the more important.

Lactic Acid, $CH_3.CH(OH).COOH$

Preparation.—(1) It can be synthesised from propionic acid by acting upon it with bromine, and then hydrolysing the α-bromo-propionic acid obtained by boiling with dilute alkalies:

$$CH_3.CH_2.COOH \longrightarrow CH_3.CHBr.COOH \longrightarrow CH_3.CH(OH).COOH.$$

(2) Lactic acid is present in sour milk, being produced by the fermentation of the milk sugar by various micro-organisms which gain access from the atmosphere. It is manufactured by the fermentation of solutions of glucose by *Bacillus acidi lactici*, which is originally isolated as a pure culture from sour milk. The temperature of the fermenting liquid is kept at 45-55°. As the fermentation proceeds, the liquid is kept nearly neutral by the addition of successive small quantities of calcium carbonate, since the action of the bacillus is inhibited in strongly acid solution.

[1] See also p. 267.

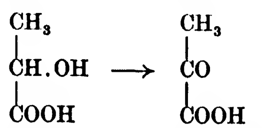
After several days the process of fermentation is complete. The liquid, which contains calcium lactate, is heated to boiling, filtered, and treated with sulphuric acid to precipitate the calcium as sulphate :

$$[CH_3.CH(OH).COO]_2Ca + H_2SO_4 = 2CH_3.CH(OH).COOH + CaSO_4.$$

The calcium sulphate is filtered off, and the filtrate evaporated to a syrup.

Properties.—Commercial lactic acid is a sour, viscous liquid, but the pure compound forms crystalline masses, melting at 18°, and boiling at 120° with decomposition. It is miscible with water in all proportions.

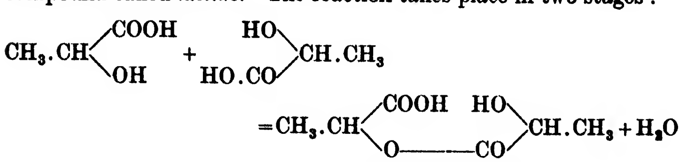
As well as being a carboxylic acid, lactic acid is a secondary alcohol (p. 225), since its molecule contains the group $>$CH.OH. On oxidation it yields a compound which is both an acid and a ketone :



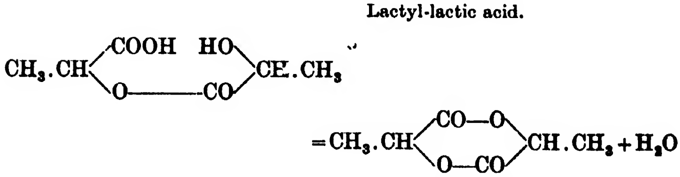
Lactic acid. Pyruvic acid.

Calcii Lactas, $[CH_3.CH(OH).COO]_2Ca,5H_2O$, is official, and has been previously described (p. 106).

Lactides and Lactones.—When lactic acid is heated, two molecules condense together, with elimination of water, to form an ester-like compound called *lactide*. The reaction takes place in two stages :



Lactyl-lactic acid.



Lactide.

The tendency to lose one or more molecules of water on heating is a characteristic not only of lactic acid but of hydroxy-carboxylic acids in general. The nature of the reaction in the case of any

particular acid is dependent upon the relative positions of the —OH and —COOH groups in the molecule, and the following general rules may be stated:

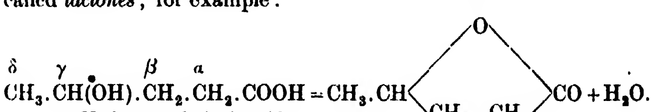
(1) In the case of α-hydroxy-acids, two molecules of the acid generally condense together, with elimination of two molecules of water and formation of lactides. Lactic acid is a typical example.

(2) β-hydroxy-acids lose a molecule of water from one molecule of the acid, with formation of an unsaturated acid; for example:

$$CH_2(OH).CH_2.COOH = CH_2:CH.COOH + H_2O.$$

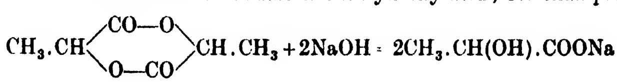
Hydracrylic acid. Acrylic acid.

(3) In the case of γ- and δ-hydroxy-acids, the —OH and —COOH groups of one molecule of the acid generally condense together, with elimination of a molecule of water and formation of compounds called *lactones*; for example:



γ-Hydroxy-valerianic acid. γ-Valero-lactone.

Both lactides and lactones are similar in chemical properties to the esters. They are neutral substances, and are insoluble in cold dilute alkalies. When boiled with alkalies they undergo hydrolysis, with formation of the alkali salt of the hydroxy-acid; for example:



Lactide. Sodium lactate.

ACIDUM LACTICUM

Lactic Acid

This is an aqueous solution, and is required to contain not less than 75 per cent by weight of lactic acid, $C_3H_6O_3$, and not less than 10 per cent by weight of lactide, $C_6H_8O_4$.

Properties.—A colourless, syrupy, hygroscopic liquid, acid to litmus. Miscible in all proportions with water, alcohol (90 per cent), and ether; almost insoluble in chloroform. Specific gravity about 1·21.

When warmed with potassium permanganate it undergoes oxidation, yielding an odour of aldehyde.

Tests for Impurities. *Copper.*—Dilute, add excess of ammonium hydroxide, and filter. The filtrate should have no blue tinge, and, on acidification with acetic acid and addition of potassium ferrocyanide, should not acquire a brown colour.

Iron.—Dilute well, and add dilute nitric acid followed by potassium ferrocyanide. There should be no blue or green colour.

Sulphate.—Dilute, acidify with hydrochloric acid, and add barium chloride, when there should be no turbidity.

Chloride.—Dilute, acidify with dilute nitric acid, and add silver nitrate, when there should be no opalescence.

Phosphate, Tartrate, Citrate, and Oxalate.—Dilute, add excess of lime water, and boil for two minutes. There should be no precipitate. Phosphate and oxalate, if present, will be precipitated at once in the cold, tartrate on standing, and citrate only on boiling.

Sarco-lactic Acid (p. 293).—Dilute, and add copper sulphate, when there should be no precipitate.

Various Sugars.—Dilute, add excess of Fehling's solution, and boil for ten minutes. There should not be more than the slightest precipitate of cuprous oxide.

Glycerin.—Add excess of zinc carbonate, evaporate to dryness, cool, and extract with absolute alcohol. The alcoholic solution, filtered and evaporated, should leave no sweet residue. This test depends upon the insolubility of zinc lactate in alcohol.

Fatty Acids.—When gently warmed it should yield no rancid odour.

Gum, Sugars, Mannite, and Calcium Phosphate.—Add the acid, drop by drop, to twice its volume of ether, when there should be no turbidity, permanent or transient.

Malic and Sulphuric Acids.—Dilute and add Liquor Plumbi Subacetatis, when there should be no precipitate.

Readily Carbonisable Organic Impurities.—Carefully pour the acid upon an equal volume of concentrated sulphuric acid, when there should be little or no darkening in colour.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—5 parts per million (p. 176).

Quantitative Estimation.—The free lactic acid is first estimated by titration with standard sodium hydroxide. The lactide is then determined by adding a known excess of standard sodium hydroxide, boiling until hydrolysis is complete, and back-titrating with standard acid.

Weigh about 10 grammes, dilute to 100 mils, and titrate portions of 20 mils with N/1 sodium hydroxide, using phenolphthalein as indicator:

$$NaOH + CH_3.CH(OH).COOH = CH_3.CH(OH).COONa + H_2O,$$
$$NaOH \equiv C_3H_6O_3,$$
$$40 \equiv 90,$$
$$1000 \text{ mils of N/1 } NaOH \equiv 90 \text{ grammes of } C_3H_6O_3,$$
$$1 \text{ mil N/1 } NaOH \equiv 0{\cdot}090 \text{ gramme of } C_3H_6O_3.$$

To the neutral liquid obtained in each titration add 20 mils of N/1 sodium hydroxide, and boil for fifteen minutes in order to hydrolyse all the lactide. Titrate the liquid thus obtained with N/1 sulphuric acid. The number of mils of acid required, sub-

tracted from 20, gives the number of mils of N/1 sodium hydroxide used in hydrolysing the lactide :

$$2NaOH + CH_3.CH\begin{matrix} \diagup CO-O \diagdown \\ \diagdown O-CO \diagup \end{matrix}CH.CH_3 = 2CH_3.CH(OH).COONa,$$

$$2NaOH \equiv C_6H_8O_4,$$
$$2 \times 40 \equiv 144,$$
$$1000 \text{ mils N/1 NaOH} \equiv 72 \text{ grammes of } C_6H_8O_4,$$
$$1 \text{ mil N/1 NaOH} \equiv 0{\cdot}072 \text{ gramme of } C_6H_8O_4.$$

UNSATURATED MONOCARBOXYLIC ACIDS

Acrylic acid, $CH_2:CH.COOH$, is formed when hydracrylic acid is distilled :

$$CH_2(OH).CH_2.COOH = CH_2:CH.COOH + H_2O.$$

It can also be prepared by heating β-bromo-propionic acid with alcoholic potash :

$$CH_2Br.CH_2.COOH + KOH = CH_2:CH.COOH + KBr + H_2O,$$

or by cautiously oxidising allyl alcohol (p. 282) :

$$CH_2:CH.CH_2.OH + 2O = CH_2:CH.COOH + H_2O.$$

Acrylic acid is a pungent-smelling liquid, and is a fairly strong monobasic acid. In addition it has the usual properties of an unsaturated compound. It is very easily oxidised, and can combine directly with nascent hydrogen and with the halogens :

$$CH_2:CH.COOH \xrightarrow{2\hat{H}} CH_3.CH_2.COOH \quad \text{Propionic acid.}$$

$$CH_2:CH.COOH \xrightarrow{Br_2} CH_2Br.CHBr.COOH \quad \alpha,\beta\text{-Dibromo-propionic acid.}$$

Acidum Oleicum, *Oleic Acid*, $C_{17}H_{33}.COOH$, is a high member of the series of unsaturated acids, of which acrylic is the lowest. It is derived theoretically from stearic acid by removal of two hydrogen atoms from adjacent carbon atoms in the centre of the chain, its full structural formula being :

$$\begin{array}{l} CH.CH_2.CH_2.CH_2.CH_2.CH_2.CH_2.CH_2.CH_3 \\ \| \\ CH.CH_2.CH_2.CH_2.CH_2.CH_2.CH_2.CH_2.COOH. \end{array}$$

In combination with glycerin, oleic acid is the main constituent of many fatty vegetable oils, from which it can be obtained by hydrolysis with boiling dilute alkalies or superheated steam.

When pure, oleic acid is a colourless oil, which solidifies on cooling to a solid melting at 14°. It is insoluble in water. On exposure to air it gradually becomes straw-coloured, and develops a rancid odour.

It resembles stearic acid, in that its acidic properties are very feeble; it dissolves in alkalies, with formation of salts, but when pure it is neutral to litmus.

Being an unsaturated compound, oleic acid rapidly decolorises a cold alkaline solution of potassium permanganate, and combines directly with bromine to form an additive product, $C_{17}H_{33}Br_2.COOH$. On reduction, oleic acid is converted into stearic acid:

$$C_{17}H_{33}.COOH + 2H = C_{16}H_{35}.COOH.$$

Linolic acid, $C_{17}H_{31}.COOH$, and α-**linolenic acid,** $C_{17}H_{29}.COOH$, are unsaturated acids which occur, in combination with glycerin, in the so-called "drying oils", such as Oleum Lini (p. 275). Linolic acid contains two double bonds, and α-linolenic acid contains three. The free acids and their glycerides readily undergo oxidation on exposure to air, with formation of hard, amorphous, glassy solids, and it is to this fact that drying oils owe their peculiar properties.

CHAPTER XXI

THE ESTERS, OR ETHEREAL SALTS

Ethyl Acetate, Acetic Ether, $CH_3.COOC_2H_5$

Ethyl acetate is an example of a purely organic ester (compare p. 217).

Preparation.—(1) Ethyl acetate is formed when acetyl chloride or acetic anhydride acts on ethyl alcohol:

$$CH_3.COCl + C_2H_5.OH = CH_3.COOC_2H_5 + HCl,$$
$$(CH_3.CO)_2O + 2C_2H_5.OH = 2CH_3.COOC_2H_5 + H_2O.$$

(2) It is prepared by the interaction of alcohol and glacial acetic acid, in the presence of concentrated sulphuric acid as a dehydrating agent:

$$CH_3.COOH + C_2H_5.OH = CH_3.COOC_2H_5 + H_2O.$$

A mixture of alcohol (50 mils) and concentrated sulphuric acid (50 mils) is heated to 140° in a half-litre distillation flask connected to a condenser and receiver, and a mixture of alcohol (100 mils) and glacial acetic acid (100 mils) is added drop by drop through a dropping funnel. The distillate is well shaken in a separating funnel with about half its volume of strong sodium carbonate solution, to remove acetic acid and alcohol. The ethereal layer is then dried over calcium chloride, and purified by fractional distillation from a water-bath.

Properties.—Ethyl acetate is a colourless, mobile liquid, with a pleasant, fruity odour. Specific gravity, 0·9; boiling-point, 77°. It is soluble about 1-11 in water, and is miscible with alcohol, ether, and chloroform, the solutions being neutral to indicators.

When ethyl acetate is boiled with water under a reflux condenser, it slowly undergoes hydrolysis:

$$CH_3.COOC_2H_5 + H_2O = CH_3.COOH + C_2H_5.OH.$$

The hydrolysis takes place much more rapidly if a dilute solution of an alkali, such as sodium hydroxide or sodium carbonate, is employed:

$$CH_3.COOC_2H_5 + NaOH = CH_3.COONa + C_2H_5.OH.$$

In the latter case the products of hydrolysis can be separated by

first distilling off the alcohol and then evaporating the remaining solution of sodium acetate to dryness, and recovering the acetic acid from the solid residue by distillation with concentrated sulphuric acid.

ÆTHER ACETICUS

Acetic Ether

This is required to contain not less than 90 per cent of ethyl acetate, $CH_3.COOC_2H_5$. Specific gravity, 0·900-0·907.

Tests for Impurities. *Free Acid.*—It should not immediately redden moistened blue litmus paper.

Esters derived from Fusel Oil.—A few drops allowed to evaporate from filter-paper should leave no extraneous odour.

Readily Carbonisable Organic Impurities.—When carefully poured upon concentrated sulphuric acid, no dark ring should be formed at the junction of the liquids within fifteen minutes.

Quantitative Estimation.—It is estimated by hydrolysis with standard sodium hydroxide, the excess of alkali being then determined by titration with standard sulphuric acid. In order to avoid taking any free acid present into account, the liquid is neutralised prior to hydrolysis. Weigh about 5 grammes in a stoppered weighing bottle, transfer to a flask, and make up to 100 mils with water. Neutralise a portion of 10 mils with N/1 sodium hydroxide, using phenolphthalein as indicator; add 20 mils of N/1 sodium hydroxide, set aside for five minutes, rotating occasionally, dilute with water, and titrate back with N/1 sulphuric acid. The number of mils of acid required, subtracted from 20, gives the volume of alkali required to effect the hydrolysis:

$$\underset{40}{NaOH} + \underset{88}{CH_3.COOC_2H_5} = CH_3.COONa + C_2H_5.OH, \quad 40 \equiv 88$$

$$1000 \text{ mils N/1 } NaOH \equiv 88 \text{ grammes of } CH_3.COOC_2H_5,$$

$$1 \text{ mil N/1 } NaOH \equiv 0{\cdot}088 \text{ gramme of } CH_3.COOC_2H_5.$$

Ethyl Nitrite, $C_2H_5.NO_2$

Preparation.—Ethyl nitrite is prepared by the action of nitrous acid on alcohol:

$$C_2H_5.OH + HNO_2 = C_2H_5.NO_2 + H_2O.$$

For the laboratory preparation the following procedure will be found satisfactory: 7 mils of concentrated sulphuric acid is cautiously added to 40 mils of alcohol in about 75 mils of water, and the mixture is placed in a flask, well cooled in ice. A solution of 34·5 grammes of sodium nitrite in 120 mils of water is slowly run in, with constant stirring. The ethyl nitrite separates out as a layer floating on the surface. It is separated, freed from traces of alcohol by washing with a little water, and dried over anhydrous potassium carbonate.

Properties.—Ethyl nitrite is a colourless, mobile liquid, with a pleasant, ethereal odour. Boiling-point, 16·5-17·5°; specific gravity, 0·90. It is slightly soluble in water, and miscible with alcohol.

It can be readily hydrolysed by adding it drop by drop to boiling dilute sodium hydroxide :

$$C_2H_5.NO_2 + NaOH = C_2H_5.OH + NaNO_2.$$

Ethyl nitrite is neutral to indicators when freshly prepared and pure, but, if moist, is liable to undergo decomposition on keeping, with liberation of nitrous acid. It can be preserved fairly satisfactorily if mixed with excess of dry alcohol and a little glycerin.

Liquor Ethyl Nitritis, *Solution of Ethyl Nitrite,* consists of 2·5-3 per cent by weight of ethyl nitrite dissolved in a mixture of 95 parts by volume of absolute alcohol and 5 parts by volume of glycerin. It is a nearly colourless liquid, of specific gravity 0·823-0·826, and has the characteristic odour of the ester. The percentage of ethyl nitrite in the solution can be estimated by means of nitrometer, exactly as described under Spiritus Ætheris Nitrosi.

SPIRITUS ÆTHERIS NITROSI

Spirit of Nitrous Ether. *Syn.* Sweet Spirit of Nitre

This is an alcoholic solution containing between 1·52 and 2·66 per cent by weight of ethyl nitrite, together with small amounts of aldehyde, nitrous acid, and other substances produced by secondary reactions during manufacture or due to decomposition on keeping.

Preparation.—Sulphuric acid, alcohol, and nitric acid are placed in a retort together with copper turnings. The mixture is then distilled at a temperature between 77° and 80°, as shown by a thermometer dipping into the liquid. If the temperature is allowed to exceed 82° the reaction is liable to become somewhat violent, and an excessive amount of aldehyde is evolved ; for this reason a sand-bath is a more suitable source of heat on the small scale than a water-bath, as the temperature is more easily controlled.

The distillate, after condensation, is passed into a vessel containing alcohol, and when the volume of liquid in the receiver has increased to a certain amount, a further quantity of nitric acid is added to the contents of the retort. The addition of the whole of the acid at first would make the reaction difficult to control and increase the quantity of aldehyde formed, whereas the later addition has a beneficial effect on the yield of ethyl nitrite. It is essential that the receiver be immersed in ice-cold water or much of the nitrite will be lost by volatilisation, since it boils at 17°.

When the liquid in the receiver has further increased to a definite volume, distillation is discontinued, and the spirit obtained is assayed prior to adjustment to such a volume with alcohol as will produce a solution of ethyl nitrite of the required strength.

In considering what reactions occur it must first be noticed that

the residue in the retort contains copper sulphate crystals and unchanged copper. Now it is known that sulphuric acid of the strength contained in the retort has little action upon copper under ordinary circumstances, so that it must be assumed that copper nitrate is first formed :

$$2HNO_3 + Cu = Cu(NO_3)_2 + 2\hat{H}.$$

The sulphuric acid then acts upon the nitrate with production of nitric acid and copper sulphate :

$$H_2SO_4 + Cu(NO_3)_2 = CuSO_4 + 2HNO_3.$$

The nascent hydrogen shown in the first equation never appears as the free gas, but reduces some of the nitric acid to nitrous acid :

$$HNO_3 + 2\hat{H} = H_2O + HNO_2,$$

and the nitrous acid then reacts with the alcohol to produce the ester, ethyl nitrite, which distils over :

$$HNO_2 + C_2H_5.OH = C_2H_5.NO_2 + H_2O.$$

Numerous secondary reactions occur with formation of aldehyde and small quantities of other substances, but these reactions are not of such importance as to claim attention here.

Quantitative Estimation.—The Pharmacopœia says : " 1 volume shaken briskly at intervals during five minutes in a brine-charged nitrometer with 1 volume of potassium iodide solution and 1 volume of diluted sulphuric acid yields at 15·5° and normal pressure not less than 4 or more than 7 volumes of nitric oxide gas, corresponding to not less than 1·52 or more than 2·66 parts by weight of ethyl nitrite in 100 parts by weight of the spirit ". The reactions which occur here are as follows : Sulphuric acid liberates hydriodic acid from the potassium iodide :

$$KI + H_2SO_4 = KHSO_4 + HI,$$

and the hydriodic acid reacts with the ethyl nitrite with liberation of nitric oxide gas :

$$2C_2H_5.NO_2 + 2HI = 2C_2H_5.OH + I_2 + 2NO.$$

Representing the whole in one equation, in its simplest form, we have :

$$KI + C_2H_5.NO_2 + H_2SO_4 = C_2H_5.OH + KHSO_4 + NO + I.$$

For an example in working, say 1 volume of the spirit when assayed according to pharmacopœial directions yielded 6 volumes of nitric oxide gas. To what percentage of ethyl nitrite in the spirit does this correspond ?

The molecular weight of $C_2H_5.NO_2 = 75$.
" " $NO = 30$.

The gram-molecule of any gas at N.T.P. = 22·32 litres in volume,
∴ 22320 mils of NO are yielded by 75 grammes of $C_2H_5.NO_2$ at N.T.P.

$$\text{or } \frac{22320}{1} \times \frac{288 \cdot 5}{273} = 23580 \text{ mils at } 15 \cdot 5^\circ \text{ and N.P.}$$

If the sample under examination yielded 6 volumes of NO for each volume of spirit taken, then

23580 mils NO are yielded by 75 grammes of $C_2H_5.NO_2$

$$6 \quad \text{,,} \quad \text{,,} \quad \text{,,} \quad \frac{75}{23580} \times \frac{6}{1} \quad \text{,,}$$

$= 0 \cdot 019$ gramme in each mil of spirit

But we require percentage weight in weight. Say that the specific gravity of sample is 0·840 :

1 mil of spirit contains 0·019 gramme of $C_2H_5.NO_2$.

$$1 \text{ gramme} \quad \text{,,} \quad \text{,,} \quad \frac{0 \cdot 019}{0 \cdot 840} \quad \text{,,} \quad \text{,,}$$

$$100 \text{ grammes} \quad \text{,,} \quad \text{,,} \quad \frac{0 \cdot 019}{0 \cdot 840} \times \frac{100}{1} = 2 \cdot 26 \text{ per cent } w/w.$$

In carrying out this estimation a suitable quantity of spirit to use is about 5 mils.

Note.—Spirit of nitrous ether should be stored in a cool dark place, as it quickly decomposes in sunlight, and in small bottles in order that the spirit may be quickly used once the bottle has been opened. Loss of strength occurs from volatilisation and hydrolysis owing to the water present, the solution quickly becoming acid.

$$C_2H_5.NO_2 + H_2O \longrightarrow C_2H_5.OH + HNO_2.$$

For this reason the Pharmacopœia specifies that it shall effervesce not at all, or but slightly, with sodium bicarbonate solution.

It will be seen that the Liquor Ethyl Nitritis, which contains practically no water, is thus a better preparation, though it is much less commonly used.

AMYL NITRIS

Amyl Nitrite

This is prepared from amylic alcohol which has distilled between 128° and 132°. It consists chiefly of iso-amyl nitrite, $(CH_3)_2CH.CH_2.CH_2.NO_2$, together with small quantities of other alkyl nitrites.

Preparation.—35 mils of amyl alcohol is mixed with 30 grammes of solid sodium nitrite in a large flask, and well cooled in ice. To the mixture 10 mils of concentrated sulphuric acid is slowly added, drop by drop, with constant shaking. The amyl nitrite, which

separates out as a layer on top, is washed with a little water, dried over anhydrous calcium chloride, and distilled, the portion distilling between 95° and 100° being collected.

Properties.—Amyl nitrite is a pale yellow volatile liquid with a penetrating, fragrant odour. Specific gravity, 0·870-0·880. At least 90 per cent of it should distil below 100°. It is almost insoluble in water, but is miscible with alcohol.

Test for Strength.—The Pharmacopœia requires that a mixture of 5 volumes, with sufficient alcohol (90 per cent) to form 100 volumes, shall yield a liquid of which a portion tested in a nitrometer, as described under Spiritus Ætheris Nitrosi, yields not less than 7·9 times its volume of nitric oxide gas. In practice, 3 mils of the alcoholic solution should be employed.

ETHYL NITRATE, $C_2H_5 . NO_3$

This compound cannot be conveniently prepared by the action of nitric acid alone on alcohol. If concentrated nitric acid be added to alcohol in the cold, a violent and almost uncontrollable reaction rapidly sets in, torrents of brown fumes being evolved. Even if the mixture is kept carefully cooled, the nitric acid oxidises part of the alcohol, being itself reduced to nitrous acid, which then reacts with more alcohol, yielding ethyl nitrite.

Ethyl nitrate is prepared by slowly adding alcohol to concentrated nitric acid containing a little urea (p. 311), and then cautiously distilling the mixture :

$$C_2H_5.OH + HNO_3 = C_2H_5.NO_3 + H_2O.$$

The effect of the urea is to decompose any nitrous acid as soon as it is formed :

$$\underset{\text{Urea.}}{CO(NH_2)_2} + 2HNO_2 = CO_2 + 2N_2 + 3H_2O.$$

Ethyl nitrate is a colourless liquid with a fruity odour, boiling at 87°. It is sparingly soluble in water, and is rapidly hydrolysed by boiling dilute alkalies.

ETHYL HYDROGEN SULPHATE, $C_2H_5 . HSO_4$

This has been mentioned as an intermediate product in the preparation of ether and of ethylene. It can be made by heating a mixture of alcohol and concentrated sulphuric acid on a water-bath :

$$C_2H_5.OH + H_2SO_4 = C_2H_5.HSO_4 + H_2O.$$

The product is poured into water and neutralised with barium carbonate. The ethyl hydrogen sulphate is converted into its soluble barium salt, and any free sulphuric acid is precipitated as barium sulphate. After filtration the solution is treated with dilute sulphuric acid, drop by drop, until no further precipitate forms. In

this way the ethyl barium sulphate is converted into ethyl hydrogen sulphate and barium sulphate :

$$Ba(C_2H_5.SO_4)_2 + H_2SO_4 = 2C_2H_5.HSO_4 + BaSO_4.$$

The liquid is again filtered, and the clear solution of ethyl hydrogen sulphate evaporated to a syrup.

Ethyl hydrogen sulphate is a sour, viscous liquid, miscible with water. It is strongly acid in reaction, and dissolves metallic oxides, hydroxides, and carbonates forming crystalline salts, such as ethyl potassium sulphate, $C_2H_5.KSO_4$, and ethyl barium sulphate, $Ba(C_2H_5.SO_4)_2$.

Ethyl Acetoacetate, $CH_3.CO.CH_2.COOC_2H_5$

This ester is prepared by heating ethyl acetate with sodium, and then treating the product with excess of dilute hydrochloric acid. The reaction can be represented as a simple condensation of two molecules of ethyl acetate, with elimination of a molecule of alcohol :

$$CH_3.CO.OC_2H_5 + H.CH_2.COOC_2H_5 \\ = CH_3.CO.CH_2.COOC_2H_5 + C_2H_5.OH.$$

In reality the changes which take place are much more complex.

Ethyl acetoacetate is a colourless, pleasant-smelling liquid, which boils at 182°.

Under the influence of certain reagents, ethyl acetoacetate behaves as if it had the structure $CH_3.C(OH):CH.COOC_2H_5$. Thus, when treated with sodium, it is converted into a sodium derivative of the formula $CH_3.C(ONa):CH.COOC_2H_5$. This sodium derivative reacts with alkyl halides, thus :

$$CH_3.C(ONa):CH.COOC_2H_5 + R.Cl \\ = CH_3.C(OR):CH.COOC_2H_5 + NaCl,$$

$$CH_3.C(OR):CH.COOC_2H_5 = CH_3.CO.CH(R).COOC_2H_5,$$

so that the final product is an alkyl[1] derivative of ethyl acetoacetate. These alkyl derivatives undergo two interesting reactions. If boiled with dilute aqueous or alcoholic potassium hydroxide they are converted into ketones (" ketonic hydrolysis ") :

$$CH_3.CO.CH(R).COOC_2H_5 + 2KOH \\ = \underset{\text{Ketone.}}{CH_3.CO.CH_2R} + K_2CO_3 + C_2H_5.OH.$$

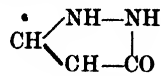
If boiled with concentrated alcoholic potash, they yield carboxylic acids (" acid hydrolysis ") :

$$CH_3.CO.CH(R).COOC_2H_5 + 2KOH \\ = CH_3.COOK + \underset{\substack{\text{Acid} \\ \text{(as potassium salt).}}}{R.CH_2.COOK} + C_2H_5.OH.$$

[1] In the equations, R represents any one alkyl group.

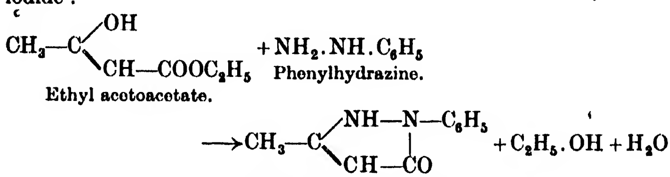
Ethyl acetoacetate is therefore a very important synthetic reagent, since, from its various alkyl derivatives, various ketones and carboxylic acids can be prepared.

Phenazonum, *Phenazone,* sometimes known as "antipyrin", is an important synthetic drug prepared from ethyl acetoacetate, and is a derivative of pyrazolone :



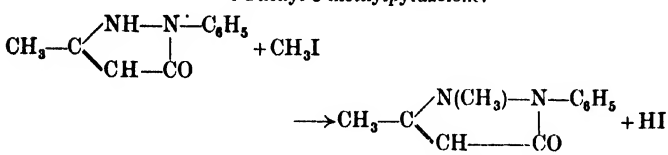
Pyrazolone.

Phenazone is prepared by heating ethyl acetoacetate with phenylhydrazine (p. 344), and then treating the product with methyl iodide :



Ethyl acetoacetate. Phenylhydrazine.

1-Phenyl-3-methylpyrazolone.



Phenazone.

Phenazone is a crystalline powder melting at 111°-113°. It is readily soluble in water and in alcohol, forming neutral solutions. With nitrous acid it gives a brilliant green colour, owing to the formation of iso-nitroso-phenazone.

CHAPTER XXII

HALOGEN COMPOUNDS

Nomenclature of Halogen Compounds.—A monohalogen derivative of a paraffin can be named in either of two ways. If it is regarded as a substitution product of the hydrocarbon, the name of the halogen is put first; if, on the other hand, it is regarded as an additive product of an alkyl radicle, then the name of the halogen is put last. Thus the compound CH_3Cl may be called either chloromethane or methyl chloride.

A similar rule applies in the case of other halogen compounds, as the following examples show:

CH_2Cl_2 . . .	Dichloromethane, or methylene dichloride.
$CH_2Br.CH_2Br$ . .	Symmetrical dibromo-ethane, or ethylene dibromide.
$CH_3.CHBr_2$ . .	Unsymmetrical dibromo-ethane, or ethylidene dibromide.
$CHBr:CHBr$ . .	Symmetrical dibromo-ethylene, or acetylene dibromide.

In the case of halogen compounds containing long carbon chains, numbers or Greek letters are often used to indicate the carbon atoms to which the halogen atoms are attached. The numbering or lettering of the carbon atoms begins at one end of the longest carbon chain. Examples of this system are:

$$\overset{\alpha}{C}H_3.\overset{\beta}{C}HI.\overset{\gamma}{C}H_3 \quad . \quad . \quad . \quad . \quad \beta\text{-Iodo-propane (iso-propyl iodide).}$$

$$\overset{1}{C}H_2Br.\overset{2}{C}H_2.\overset{3}{C}HBr.\overset{4}{C}H_3 \quad . \quad . \quad . \quad \text{1-, 3-Dibromo-butane.}$$

$$\overset{1}{C}H_3.\overset{2}{C}HCl.\overset{3}{C}H\begin{cases} CH_3 \\ \overset{4}{C}H_2.\overset{5}{C}H_3 \end{cases} \quad . \quad . \quad . \quad \text{2-Chloro-3-methyl-pentane.}$$

The position of halogen atoms in halogen-substituted carboxylic acids is indicated by Greek letters, the lettering commencing with

the carbon atom directly attached to the $-COOH$ group. For example:

$$\overset{\beta}{CH_3}.\overset{\alpha}{CHBr}.COOH \quad . \quad . \quad . \quad \alpha\text{-bromo-propionic acid.}$$

$$\overset{\beta}{CH_2Br}.\overset{\alpha}{CH_2}.COOH \quad . \quad . \quad . \quad \beta\text{-bromo-propionic acid.}$$

These few remarks on the naming of halogen substitution products also apply, in many cases, to substituent atoms or groups other than halogens.

The Alkyl Halides

From a theoretical point of view, the alkyl halides are very important compounds. They can be prepared:

1. By the action of chlorine or bromine on a paraffin hydrocarbon, a method of only theoretical interest. For example:

$$CH_4 + Cl_2 = CH_3Cl + HCl.$$

2. By the addition of a halogen acid to an olefine, another method not often employed in practice:

$$CH_2 : CH_2 + HBr = CH_3.CH_2Br.$$

3. By the action of an anhydrous halogen acid on an alcohol (esterification):

$$CH_3.OH + HCl = CH_3Cl + H_2O.$$

4. By the action of a halide of phosphorus on an alcohol:

$$C_2H_5.OH + PCl_5 = C_2H_5Cl + HCl + POCl_3,$$
$$3C_2H_5.OH + POCl_3 = 3C_2H_5Cl + H_3PO_4,$$
$$3C_2H_5.OH + PCl_3 = 3C_2H_5Cl + H_3PO_3.$$

An application of this method is used in the laboratory for preparing alkyl bromides and iodides, and consists in boiling an alcohol with bromine or iodine in the presence of red phosphorus. Tribromide or tri-iodide of phosphorus is first formed, and this then reacts with the alcohol as above.

The alkyl halides are colourless, heavy, volatile liquids, with the exception of methyl and ethyl chlorides, which are gases at ordinary temperatures. They are all insoluble or sparingly soluble in water.

Chemically, the alkyl halides are best regarded as esters of the halogen acids. Thus when boiled with water or with aqueous alkalies they undergo hydrolysis:

$$C_2H_5I + H_2O = C_2H_5.OH + HI.$$

Boiling alcoholic potash, however, converts them into olefines:

$$C_2H_5I + KOH = C_2H_4 + KI + H_2O.$$

Ethyl Chloridum, *Ethyl Chloride*, C_2H_5Cl, is the only official alkyl halide. It is generally prepared by passing dry hydrogen

chloride gas into absolute alcohol containing anhydrous zinc chloride (Groves' process):

$$C_2H_5.OH + HCl = C_2H_5Cl + H_2O.$$

The object of the zinc chloride is to take up the water formed, and so prevent the reaction from proceeding in the reverse direction.

Ethyl chloride is a colourless gas at ordinary temperatures and pressures, but can be condensed to a volatile liquid, boiling at 12°. Its specific gravity is 0·92-0·96 at 0°. It has a pleasant ethereal odour, is sparingly soluble in water, but miscible with alcohol and ether, and burns with a smoky flame.

Dihalogen Derivatives of the Paraffins

Ethylene dichloride, $CH_2Cl.CH_2Cl$, and **ethylene dibromide**, $CH_2Br.CH_2Br$, are heavy, colourless, oily, volatile liquids, prepared by the direct combination of ethylene with chlorine or bromine. Boiling alcoholic potash converts them into acetylene:

$$CH_2Br.CH_2Br + 2KOH = CH \equiv CH + 2KBr + 2H_2O.$$

When hydrolysed with dilute aqueous alkalies they yield *glycol*:

$$CH_2Cl.CH_2Cl + 2H_2O = \underset{\text{Glycol.}}{CH_2(OH).CH_2(OH)} + 2HCl.$$

Glycol is a colourless, syrupy liquid. Since it contains two —OH groups, it is known as a di-hydric alcohol, and in chemical properties it closely resembles the ordinary monohydric alcohols. On oxidation it yields a number of products, one of them being oxalic acid (p. 284):

$$\underset{\text{Glycol.}}{\begin{matrix} CH_2.OH \\ | \\ CH_2.OH \end{matrix}} + 4O = \underset{\text{Oxalic acid.}}{\begin{matrix} COOH \\ | \\ COOH \end{matrix}} + 2H_2O.$$

Ethylidene dichloride, $CH_3.CHCl_2$, is isomeric with ethylene dichloride. It can be made by the action of phosphorus pentachloride on acetaldehyde:

$$CH_3.CHO + PCl_5 = CH_3.CHCl_2 + POCl_3.$$

Chloroform, $CHCl_3$

Preparation.—(1) Chloroform can be built up from its elements, since it is one of the products of the action of chlorine on methane:

$$CH_4 + 3Cl_2 = CHCl_3 + 3HCl.$$

(2) Very pure chloroform is obtained when chloral or chloral hydrate is warmed with aqueous sodium hydroxide:

$$CCl_3.CHO + NaOH = CHCl_3 + H.COONa.$$

(3) Chloroform is generally prepared by the action of bleaching powder on aqueous alcohol or industrial spirit.

For the laboratory preparation the apparatus consists of a two-litre round-bottomed flask supported on a tripod and gauze, and connected by means of a bent tube to a condenser and receiver. Fresh bleaching powder (100 grammes) is ground into a thin paste with water (200 mils) in a large mortar and poured into the flask, any of the mixture adhering to the mortar being rinsed into the flask with a further quantity of water (200 mils). Alcohol (50 mils) is then added, and the flask is cautiously heated, the heating being discontinued as soon as the somewhat vigorous reaction begins. The liquid continues to boil and froth without further application of heat, and chloroform, together with water and a little alcohol, distils. When the reaction has subsided the contents of the flask are gently boiled until a little of the distillate, collected separately, is free from oily drops of chloroform.

The distillate is poured into a separating funnel, and the heavy layer of chloroform is run off, washed with an equal volume of water, separated again, dried over a few small lumps of anhydrous calcium chloride, and finally distilled from a water-bath.

The reactions which occur during the preparation of chloroform by this method are complex. The bleaching powder probably acts first as an oxidising agent, converting the alcohol into acetaldehyde :

$$C_2H_5.OH + Ca(OCl)Cl = CH_3.CHO + H_2O + CaCl_2.$$

The aldehyde is then chlorinated by more of the bleaching powder yielding chloral :

$$CH_3.CHO + 3Cl_2 = CCl_3.CHO + 3HCl.$$

Finally, the chloral is decomposed by the calcium hydroxide present in the bleaching powder, yielding chloroform :

$$2CCl_3.CHO + Ca(OH)_2 = 2CHCl_3 + \underset{\text{Calcium formate.}}{(H.COO)_2Ca}.$$

(4) Instead of alcohol, acetone can be used in the above preparation. The acetone is first chlorinated by the bleaching powder, yielding tri-chloracetone, and this compound is then decomposed by the calcium hydroxide present, giving chloroform :

$$(CH_3)_2CO + 3Cl_2 = CH_3.CO.CCl_3 + 3HCl,$$
$$2CH_3.CO.CCl_3 + Ca(OH)_2 = 2CHCl_3 + \underset{\text{Calcium acetate.}}{(CH_3.COO)_2Ca}.$$

Properties.—Chloroform is a colourless, heavy, volatile liquid, having a pleasant smell and a sweet, pungent taste. Specific gravity, 1·5 ; boiling-point, 61°. It is not easily inflammable, but can be made to burn with a green-edged flame.

Boiling alcoholic potash decomposes chloroform, with production of potassium formate and potassium chloride :

$$CHCl_3 + 4KOH = H.COOK + 3KCl + 2H_2O.$$

When a drop of chloroform is warmed with a drop of aniline and a little aqueous or alcoholic potash, a disgusting smell of phenyl carbylamine or phenyl isocyanide will be noticed :

$$CHCl_3 + C_6H_5.NH_2 + 3KOH = \underset{\text{Phenyl carbylamine.}}{C_6H_5.NC} + 3KCl + 3H_2O.$$

This is known as the " carbylamine reaction ", and is a very delicate test for chloroform.

CHLOROFORMUM

Chloroform

This consists of pure chloroform to which 2 per cent of absolute alcohol has been added. Ordinary chloroform is slowly oxidised by air, especially under the influence of sunlight, with formation of highly poisonous carbonyl chloride (phosgene gas) :

$$2CHCl_3 + O_2 = \underset{\text{Carbonyl chloride.}}{2COCl_2} + 2HCl$$

The alcohol is added in order to decompose any carbonyl chloride as soon as it is formed :

$$COCl_2 + 2C_2H_5.OH = \underset{\text{Ethyl carbonate.}}{CO(O.C_2H_5)_2} + 2HCl.$$

Chloroform should be kept in a well-stoppered bottle, and in a cool dark place.

Tests for Impurities.—*Non-volatile Matter.* It should evaporate without residue.

Volatile Organic Impurities.—It should not begin to boil below 60°.

Fusel Oil and Tarry Matter.—Allow 10 mils to evaporate from a large piece of filter-paper placed on a warm plate. No foreign odour should be perceptible at any stage of the evaporation.

Free Acid.—Water, shaken with half its volume of chloroform for five minutes and then separated, should be neutral to litmus.

Free Chlorine and Chloride.—A portion of the aqueous layer from the last test should give no blue colour on addition of a solution of cadmium iodide and starch mucilage (absence of free chlorine). Another portion should yield not more than a very slight opalescence on addition of silver nitrate (absence of chloride).

Readily Carbonisable Organic Impurities and Extraneous Organic Chlorine Compounds.—After shaking concentrated sulphuric acid with twice its volume of chloroform for five minutes, and setting aside for fifteen minutes, both the acid and the chloroform should

be nearly colourless. 2 mils taken from the sulphuric acid layer and diluted with 5 mils of water should remain very nearly colourless, and have a pleasant odour. When this acid liquid is further diluted with 10 mils of water and stirred with a glass rod, it should be transparent and colourless, and the addition of a few drops of silver nitrate solution should cause not more than a slightly diminished transparency. Water, which has been shaken with half its volume of chloroform, previously treated with sulphuric acid as described above, should yield not more than a slightly diminished transparency on addition of silver nitrate.

IODOFORMUM

Iodoform, CHI_3

Preparation.—(1) Iodoform is generally prepared by the action of sodium hypoiodite (or of iodine dissolved in sodium hydroxide or carbonate) on ethyl alcohol. The reactions which take place are probably analogous to those which occur during the preparation of chloroform from bleaching powder and alcohol.

To a solution of sodium carbonate crystals (10 grammes) in water (50 mils) 3 mils of alcohol are added. The solution is heated to about 70°, and iodine (5 grammes) is slowly added, with constant stirring. The liquid is cooled, and the precipitated iodoform is filtered off and purified by recrystallisation from dilute alcohol.

(2) Instead of ethyl alcohol, acetone or certain other ketones can be used in the above preparation. Methyl alcohol, it should be noted, cannot be used, and this provides a method by which methyl alcohol can be distinguished from ethyl.

Properties.—Iodoform is generally met with in small, glistening, pale yellow hexagonal plates, having a very characteristic and persistent odour. It melts at 120°, sublimes readily, and is volatile in steam. It is almost insoluble in cold water, sparingly in alcohol, and readily in chloroform and ether.

Tests for Impurities. *Non-volatile Solids.*—On ignition it should leave no appreciable ash.

Soluble Colouring Matters and Picric Acid.—Shake 1 gramme with 10 mils of water, and filter. The filtrate should have no yellow tinge and no bitter taste.

Iodide.—The filtrate from the last test, acidified with nitric acid, should yield no opalescence with silver nitrate.

Carbon Tetrachloride, CCl_4

Carbon tetrachloride is the final product of the action of chlorine on methane. It is manufactured by the action of chlorine on carbon disulphide, a trace of iodine being used as catalyst:

$$CS_2 + 3Cl_2 = CCl_4 + S_2Cl_2.$$

Carbon tetrachloride is a heavy liquid boiling at 76°, and is practically insoluble in water. It will not burn, and its heavy vapour extinguishes a flame. Boiling alcoholic potash decomposes it with formation of potassium chloride and potassium carbonate:

$$CCl_4 + 6KOH = 4KCl + K_2CO_3 + 3H_2O.$$

CHAPTER XXIII

FATS, WAXES, SOAPS, AND GLYCERIN

The familiar substance glycerin, or glycerol, is a derivative of propane, of the formula :

$$\begin{array}{l} CH_2.OH \\ | \\ CH.OH \\ | \\ CH_2.OH. \end{array}$$

Its molecule contains three —OH groups, and it is therefore known as a *trihydric* alcohol.

Like other alcohols, glycerin is capable of reacting with acids to form esters, the hydrogen atoms of the —OH groups being displaced by acid radicles. These esters are known as *glycerides*. A simple compound of this type is the glyceride of acetic acid, which is called glyceryl triacetate, or simply triacetin :

$$\begin{array}{l} CH_2.O.CO.CH_3 \\ | \\ CH.O.CO.CH_3 \\ | \\ CH_2.O.CO.CH_3. \end{array}$$

Triacetin.

Similarly, the glyceryl esters of palmitic, stearic, and oleic acids are called respectively tripalmitin, tristearin, and triolein :

$$\begin{array}{lll} CH_2.O.CO.C_{15}H_{31} & CH_2.O.CO.C_{17}H_{35} & CH_2.O.CO.C_{17}H_{33} \\ | & | & | \\ CH.O.CO.C_{15}H_{31} & CH.O.CO.C_{17}H_{35} & CH.O.CO.C_{17}H_{33} \\ | & | & | \\ CH_2.O.CO.C_{15}H_{31}. & CH_2.O.CO.C_{17}H_{35}. & CH_2.O.CO.C_{17}H_{33}. \\ \text{Tripalmitin.} & \text{Tristearin.} & \text{Triolein.} \end{array}$$

FATS AND OILS

Animal fats, such as lard and suet, and " fixed " or fatty vegetable oils, such as olive oil, almond oil, and oil of theobroma, consist essentially of mixtures of tripalmitin, tristearin, and

triolein in varying proportions. Tripalmitin and tristearin are solid at ordinary temperatures, but triolein is an oily liquid. It is evident, therefore, that the difference in hardness between the various kinds of fats and oils depends largely on the proportions of these three main constituents. Thus liquid vegetable oils contain relatively large proportions of triolein as compared with solid animal fats. It may be remarked that there is no sharp dividing line between solid fats and liquid oils; "cocoanut oil", for example, is liquid in tropical countries, but is generally quite solid in England.

Fats and fixed oils of all kinds have certain characteristics in common. They are all greasy substances, which float on water. They are insoluble in water, sparingly soluble in alcohol, and readily soluble in ether, chloroform, and benzene. They cannot be distilled, and on heating they decompose, emitting the characteristic odour of scorched fat (due to the formation of acrolein, p. 283). Many fats and oils slowly turn rancid on long exposure to air, becoming acid in reaction and developing a very disagreeable odour.

Sevum Præparatum, *Prepared Suet*, is the purified internal fat of the abdomen of the sheep. In its preparation, ordinary suet or "rough fat" is heated with water in large lead-lined tanks, in order to separate the fat from membranous matter. On allowing to settle, the molten fat rises to the surface as a clear layer, and is drawn off.

Prepared suet consists of about 70-80 per cent of tripalmitin and tristearin, and about 20-30 per cent of triolein.

Adeps Præparatus, *Prepared Lard*, is the purified internal fat of the hog, and is obtained in a similar way to that described for prepared suet.

Prepared lard contains the same constituents as prepared suet, but the proportion of triolein is greater (about 50-60 per cent), thus rendering it much more soft.

Oleum Morrhuæ, *Cod-liver Oil*, contains tripalmitin and tristearin, together with the glycerides of two unsaturated acids, known as jecoleic and therapic acids. The nutrient properties of the oil are attributed largely to the presence of these unsaturated glycerides and of fat soluble vitamin A, which is also present in considerable quantity.

Oleum Olivæ, *Olive Oil*, consists chiefly of triolein (80 per cent and upwards), tripalmitin, and small quantities of other glycerides. It contains no tristearin. **Oleum Sesami,** *Sesame Oil*, and **Oleum Amygdalæ,** *Almond Oil*, also consist principally of triolein. **Oleum Theobromatis,** *Oil of Theobroma*, which is solid at ordinary temperatures, contains tripalmitin and tristearin, in addition to triolein and other glycerides.

Oleum Lini, *Linseed Oil*, is a well-known example of what is called a "drying oil". Such oils contain considerable proportions of glycerides of highly unsaturated acids, such as linolic and linolenic acids. When the oil is exposed to air in thin layers, these

glycerides become oxidised, and the oil dries to a hard, transparent varnish, known as linoxyn.

Criteria of Purity of Fats and Oils.—Many fats and oils are variable in quality, and are also liable to adulteration by cheaper varieties. It is not, as a rule, possible to determine the purity of a fat or oil by an estimation of any one chemical constituent, and evidence of quality is usually dependent upon the determination of certain arbitrary chemical constants. The more important of these are as follow:

The Acid Value.—This is a number indicating the amount of the free acids present, and is determined by titrating an alcoholic solution of the fat or oil with N/10 potassium hydroxide. Fats which have become stale and rancid have abnormally high acid values, owing to partial decomposition of the glycerides with liberation of free acids. The acid value is therefore a valuable test for freshness.

The Saponification Value is the number of milligrams of potassium hydroxide required to effect the complete saponification of the fat or oil, and is determined by boiling with a known excess of standard alcoholic potash, and afterwards titrating back with standard hydrochloric acid. In the case of most pure fats and oils the saponification value lies between about 190 and 200. Waxes have much lower saponification values—about 120.

The Iodine Value is the proportional weight of iodine absorbed by 100 parts by weight of the oil or fat, under certain specified conditions. The absorption of iodine is due to direct addition to double bonds, and the iodine value thus gives an indication of the relative proportions of unsaturated acids (oleic, linolic, linolenic, etc.) in different fats and oils. For this reason solid fats (and waxes) have very low iodine values; non-drying oils have iodine values of about 80-100, and drying oils have very high iodine values. This will be apparent from the following table, which gives the iodine values of a few typical official substances, and, for comparison, those of the commoner unsaturated acids:

	Iodine Value.
Oleic Acid	80
Linolic Acid	181
Linolenic Acid	274
Cetaceum	3-4·4
Sevum Præparatum	33-46
Adeps Præparatus	52-63
Oleum Olivæ	79-87
Oleum Ricini	83-90
Oleum Morrhuæ	155-173
Oleum Lini	Not less than 170 (about 170-200).

Waxes

Waxes are composed mainly of esters of fatty acids, but differ from fats and oils in that the acids are combined, not with glycerin, but with certain of the higher monohydric alcohols.

Cera Flava, *Yellow Beeswax*, is obtained from the honeycomb of the hive bee, and is a yellowish-brown solid, which becomes plastic by the heat of the hand. It consists largely of miricyl palmitate, $C_{15}H_{31}.COOC_{30}H_{61}$. **Cera Alba,** *White Beeswax*, is prepared by bleaching the yellow variety. This is done either by exposing the wax, in thin layers, to the action of air, moisture, and sunlight, or by treating it with chemical oxidising agents, such as acidified potassium dichromate.

Cetaceum, *Spermaceti*, is a solid wax obtained from the sperm whale. It forms white, glistening, translucent masses, with a crystalline fracture, and consists chiefly of cetyl palmitate, $C_{15}H_{31}.COOC_{16}H_{33}$.

Adeps Lanæ, *Wool Fat*, is the purified fat of sheep wool, freed from water. Strictly speaking, it is not a fat, but a complex waxy mixture, consisting principally of esters of the two complex monohydric alcohols, cholesterol and isocholesterol.

Soaps

When a fat or fatty oil is boiled with a solution of sodium hydroxide it undergoes hydrolysis, the products being free glycerin and a mixture of the sodium salts of the various fatty acids. The following equation represents the reaction in the case of tristearin:

$$\begin{array}{lcl} CH_2.O.CO.C_{17}H_{35} & & CH_2.OH \\ | & & | \\ CH.O.CO.C_{17}H_{35} + 3NaOH & = & CH.OH + 3C_{17}H_{35}.COONa. \\ | & & | \\ CH_2.O.CO.C_{17}H_{35} & & CH_2.OH \\ \text{Tristearin.} & & \text{Glycerin.} \quad \text{Sodium stearate.} \end{array}$$

Soaps are the mixtures of the sodium salts of the fatty acids formed in this way. The process of the conversion of fats into soaps is called " saponification ". This term is sometimes applied, in a rather loose way, to the hydrolysis of any ester by an alkali. Thus ethyl acetate is sometimes said to be " saponified " by sodium hydroxide, although no true soap is formed in the reaction.

Sapo Animalis, *Curd Soap*.—In the preparation of curd soap, purified animal fat is boiled for a considerable time with aqueous caustic soda in a large cylindrical vessel called a " soap kettle ". When the hydrolysis is complete, dry salt is added. Soap is only sparingly soluble in brine, so that, as the salt dissolves, the soap separates from the hot solution in the liquid form, and floats on the top. The aqueous layer underneath, containing salt, glycerin, and

any excess of caustic soda, is run off, and the soap, after purification by special methods, is allowed to solidify in moulds.

Curd soap consists chiefly of sodium stearate and sodium palmitate, with not more than 30 per cent of water. If it is dissolved in water and the solution acidified with hydrochloric acid, the free fatty acids are precipitated in the form of a white curd. For example:

$$\underset{\text{Sodium palmitate.}}{C_{15}H_{31}.COONa} + HCl = \underset{\text{Palmitic acid.}}{C_{15}H_{31}.COOH} + NaCl.$$

Sapo Durus, *Hard Soap*, is prepared in a similar manner from olive oil. It consists largely of sodium oleate, with smaller quantities of sodium palmitate, and not more than 30 per cent of water.

Sapo Mollis, *Soft Soap*, is prepared by boiling olive oil with a solution of caustic potash. This soap cannot be " salted out ", as the salt and soap would react to form potassium chloride and ordinary soda soap. The solution, after hydrolysis, is therefore simply boiled down until, on cooling, it sets to a clear, soft, translucent jelly. Soft soap thus contains much of the glycerin produced during the saponification.

Tests for Impurities in Official Soaps. *Alkaline Hydroxides and Free Fatty Acids.*—It is useless to test an aqueous solution of a soap for free acid or alkali, since a soap is invariably alkaline in solution owing to partial hydrolysis. The test is therefore carried out in alcoholic solution. Dissolve 5 grammes of the dried soap in 50 mils of boiling alcohol (90 per cent), filter the hot solution, and wash the filter thoroughly with boiling alcohol. The mixed filtrate and washings should be neutral to phenolphthalein.

Alkali Carbonates (Limit of).—This test depends on the fact that alkali carbonates are insoluble in alcohol. Wash the filter-paper from the above test with boiling water. The washings should require for neutralisation not more than 5 mils of N/10 sulphuric acid, using methyl orange as indicator.

Free Fats and Oils.—The soaps should not impart a greasy stain to white unglazed paper.

Potassium (in Sodium Soaps).—The ash obtained on ignition of Sapo Animalis and Sapo Durus should not be deliquescent.

Foreign Fatty Acids (in Olive Oil Soaps).—Dissolve the soap in hot water, add a slight excess of hydrochloric acid, and heat on a water-bath until the liberated fatty acids form a transparent layer. Separate the fatty acids on a wet filter-paper, and wash with hot water until the washings are neutral to methyl orange. Filter the oily layer through a dry filter-paper in a warm oven. The fatty acids thus obtained should have the following characters: Iodine value, 83-92; acid value, 195-205; melting-point, 21-28°; refractive index at 40°, 1·454-1·458. The separation of the molten fatty acids depends upon the fact that they will pass through a dry filter-paper, but not through a wet one.

Substances Similar to Soaps

Zinci Oleostearas, *Zinc Oleostearate*, is a zinc "soap". It is prepared by mixing a solution of hard soap and curd soap with a solution of zinc sulphate. The zinc soap is formed by double decomposition, and, being insoluble in water, is precipitated.

Hydrargyrum Oleatum, *Oleated Mercury*, may be regarded as a mercury soap in that it consists principally of mercuric oleate. It is a yellow, unctuous substance, and is prepared by triturating yellow mercuric oxide with a little liquid paraffin, adding oleic acid, and heating at 50° with occasional trituration, until combination has been effected.

Emplastrum Plumbi, *Lead Plaster*, is made by heating a mixture of litharge, olive oil, and water, when the triolein is hydrolysed with formation of lead oleate and glycerin. Before drying, the mass is kneaded with hot water to remove glycerin.

Glycerin, Glycerol, $C_3H_5(OH)_3$

Preparation.—(1) Glycerin can be synthesised from ethyl alcohol (which can itself be built up from its elements, see p. 218) by the following series of reactions :

$$\underset{\text{Ethyl alcohol}}{CH_3.CH_2.OH} \xrightarrow{\text{oxidation}} \underset{\text{Acetic acid.}}{CH_3.COOH} \xrightarrow{\text{heat calcium salt}} \underset{\text{Acetone.}}{CH_3.CO.CH_3},$$

$$\xrightarrow{\text{reduction}} \underset{\text{Isopropyl alcohol.}}{CH_3.CH(OH).CH_3} \xrightarrow[\text{sulphuric acid}]{\text{heat with conc.}} \underset{\text{Propylene.}}{CH_3.CH:CH_2},$$

$$\xrightarrow{\text{addition of chlorine}} \underset{\text{Propylene dichloride.}}{CH_3.CHCl.CH_2Cl},$$

$$\xrightarrow{\text{action of chlorine in presence of a catalyst}} \underset{\text{Glyceryl trichloride.}}{CH_2Cl.CHCl.CH_2Cl},$$

$$\xrightarrow{\text{hydrolysis}} \underset{\text{Glycerin.}}{CH_2(OH).CH(OH).CH_2(OH)}.$$

(2) The glycerin of commerce is largely prepared from the waste liquor obtained, as previously described, during the manufacture of soda soaps. The liquor, which contains from 4 to 9 per cent of glycerin, is neutralised, filtered, and heated in vacuum pans. The water distils off, leaving the glycerin and salt. The glycerin is then separated by filtration, and purified by distillation under diminished pressure.

Another process for the manufacture of glycerin from fats consists in hydrolysing the fats by heating with water under pressure :

$$\text{Fats} + \text{water} = \text{fatty acids} + \text{glycerin.}$$

Properties.—Glycerin is a sweet, viscous, colourless liquid, of specific gravity 1·26. When obtained absolutely pure and free from all traces of water, it forms colourless crystals, melting at 17°. The crystals are very hygroscopic, and small traces of water-vapour, absorbed from the air, are sufficient to convert it into the ordinary syrupy form. Glycerin mixes in all proportions with water and with alcohol, but is insoluble in ether. It boils at about 290°.

In chemical properties glycerin is very similar to the monohydric alcohols. Thus it is readily acted upon by sodium, with evolution of hydrogen and formation of a solid sodium derivative. Being a trihydric alcohol, it can form esters by interaction with one, two, or three equivalents of an acid. Thus, by heating it at different temperatures with different quantities of acetic acid, the following esters can be prepared :

$C_3H_5(OH)_2.O.CO.CH_3$	Monacetin.
$C_3H_5(O.CO.CH_3)_2.OH$	Diacetin.
$C_3H_5(O.CO.CH_3)_3$	Triacetin.

As in the case of the monohydric alcohols, the —OH groups in glycerin can be displaced by chlorine atoms. Thus, hydrochloric acid converts glycerin first into α-monochlorohydrin and then into αα′-dichlorohydrin. Either of these compounds, on treatment with phosphorus pentachloride, yields glyceryl trichloride :

$$\begin{array}{llllllll}
\alpha & CH_2.OH & & CH_2Cl & & CH_2Cl & & CH_2Cl \\
 & | & & | & & | & & | \\
\beta & CH.OH & \longrightarrow & CH.OH & \longrightarrow & CH.OH & \longrightarrow & CHCl \\
 & | & & | & & | & & | \\
\alpha' & CH_2.OH & & CH_2.OH & & CH_2Cl & & CH_2Cl. \\
 & \text{Glycerin.} & & \alpha\text{-Monochloro-} & & \alpha\alpha'\text{-Dichloro-} & & \text{Glyceryl} \\
 & & & \text{hydrin.} & & \text{hydrin.} & & \text{trichloride.}
\end{array}$$

Glycerin can be distilled unchanged under diminished pressure, but if distilled at ordinary pressures it is partially decomposed, with evolution of pungent vapours containing acrolein (p. 283).

Glycerin is readily attacked by potassium permanganate and other oxidising agents, with formation of a variety of products, including carbon dioxide and oxalic acid.

GLYCERINUM

Glycerin

This consists of glycerin, associated with a small quantity of water. It should be colourless, odourless, and neutral to litmus. Specific gravity, 1·260.

In the Pharmacopœia there are nine preparations consisting of solutions of various substances in glycerin. The reasons underlying the use of glycerin in these preparations may be summarised as follows:

1. Glycerin dissolves many substances which are not very readily soluble in water, such as borax, boric acid, and phenol.

2. It is viscous and hygroscopic, and it therefore maintains in a moist condition surfaces to which it is applied, and also adheres to mucous surfaces; in this way the dissolved medicament is ensured a prolonged contact with the affected part, and its penetrative action is increased.

3. It acts as an antiseptic and preservative, though not to the extent formerly believed.

When used for extracting the proximate constituents of drugs, glycerin suffers from the same disadvantages as water, in that it dissolves gummy and albuminous matter, and tends to extract a large amount of tannin. The solubility of tannin and its oxidation products in glycerin is sometimes, however, of considerable use in pharmacy.

Tests for Impurities. *Non-volatile Solids.*—On ignition it should yield no appreciable ash.

Lead.—When tested according to the quantitative limit-test (p. 173), but using 10 grammes in each Nessler glass, no difference should be observed on adding the sodium sulphide to one of the solutions.

Copper.—When the above test is repeated, but omitting the addition of ammonium hydroxide and potassium cyanide, and adding to each solution 1 mil of dilute hydrochloric acid, no difference in colour should be observed on passing hydrogen sulphide through one of the solutions.

Iron (Limit of).—A mixture of 10 mils of glycerin with 40 mils of water, 1 drop of Solution of Ammonia, and 1 drop of a freshly prepared 10 per cent solution of tannic acid should assume not more than a faint and transient pink or purple coloration.

Ammonium.—Dilute with water, add sodium hydroxide, boil, and test the evolved vapours with turmeric paper.

Sulphate.—A 1-10 aqueous solution, acidified with hydrochloric acid, should give no turbidity on addition of barium chloride.

Chloride.—A 1-10 aqueous solution, acidified with dilute nitric acid, should not become opalescent on addition of silver nitrate.

Sugar.—When gradually heated it should assume not more than a faint yellow, but no pink, coloration, and should yield not more than a very slight charred residue and no odour of burnt sugar.

Formic Acid and Acrolein.—When mixed with an equal volume of Solution of Ammonia and a few drops of silver nitrate solution, and set aside in a dark place for five minutes, no darkening in colour should take place.

Fatty Acids.—Warm with an equal volume of dilute sulphuric acid and shake the mixture vigorously, when not more than a faint odour should be noticeable.

Extraneous Organic Matter.—When shaken with an equal volume of concentrated sulphuric acid, the mixture being kept well cooled, not more than a very slight straw coloration should be produced.

Arsenic Limit.—4 parts per million (p. 176).

Derivatives of Glycerin

Nitroglycerin, $CH_2(NO_3).CH(NO_3).CH_2(NO_3)$, or, more correctly, glyceryl trinitrate, is the glyceride of nitric acid. It is prepared by slowly adding glycerin to an ice-cooled mixture of concentrated sulphuric acid (4 parts) and concentrated nitric acid (1 part). The solution is cautiously run into ice-cold water, when the nitroglycerin separates as a heavy oil, which is purified by repeated washing with cold water.

Nitroglycerin is a heavy, colourless oil, with a sweetish taste; it is practically insoluble in water and in alcohol, but readily soluble in ether. Pure nitroglycerin is an exceedingly dangerous substance to handle. It explodes with great violence if rapidly heated or struck with a hammer, and, if impure, it is liable to explode spontaneously. Nitroglycerin is used in the manufacture of dynamite and of blasting gelatine, which are comparatively safe explosives. In pharmacy it is used in making Tabellæ Trinitrini and Liquor Trinitrini.

The Allyl Compounds.—Compounds of this class contain the unsaturated allyl radicle, $CH_2:CH.CH_2—$. As most of these compounds are prepared from glycerin, it is convenient to consider them here.

Allyl alcohol, $CH_2:CH.CH_2.OH$, is prepared by heating a mixture of glycerin and oxalic acid, in a retort, to 250°. The reaction takes place in the following stages:

$$\begin{array}{llll} CH_2.OH & CH_2.O.CO.COOH & CH_2.O.CHO & CH_2 \\ | & | & | & \| \\ CH.OH \longrightarrow & CH.OH & \longrightarrow CH.OH & \longrightarrow CH \\ | & | & | & | \\ CH_2.OH & CH_2.OH & CH_2.OH & CH_2.OH. \\ \text{Glycerin.} & \text{Monoxalin.} & \text{Monoformin.} & \text{Allyl alcohol.} \end{array}$$

This preparation should be carefully compared with that of formic acid (p. 244). The same ingredients are employed in both cases, but, if allyl alcohol is required, a sufficiently high temperature is employed to bring about the decomposition of the monoformin, as shown above.

Allyl alcohol is a colourless liquid with an irritating odour. It has the properties both of an unsaturated compound and of an

alcohol. As an unsaturated compound, it can combine directly with nascent hydrogen and with the halogens. For example:

$$CH_2:CH.CH_2.OH+2\hat{H}=CH_3.CH_2.CH_2.OH.$$

Propyl alcohol.

$$CH_2:CH.CH_2.OH+Br_2=CH_2Br.CHBr.CH_2.OH.$$

$\alpha\beta$-Dibromohydrin.

As an alcohol it forms a sodium derivative, $CH_2:CH.CH_2.ONa$, on treatment with metallic sodium; it is acted upon by bromides or iodides of phosphorus, with formation of allyl bromide, $CH_2:CH.CH_2Br$, or allyl iodide, $CH_2:CH.CH_2I$; and, on oxidation, it is converted first into an aldehyde and then into a carboxylic acid:

$$\underset{\text{Allyl alcohol.}}{CH_2:CH.CH_2.OH}\longrightarrow\underset{\text{Acrolein.}}{CH_2:CH.CHO}\longrightarrow\underset{\text{Acrylic acid.}}{CH_2:CH.COOH.}$$

Acrolein, $CH_2:CH.CHO$, is formed by oxidation of allyl alcohol, and, in small quantities, when glycerin is distilled. It is usually prepared by heating glycerin with potassium hydrogen sulphate, which, by raising the boiling-point, assists the decomposition of the glycerin:

$$\underset{\text{Glycerin.}}{\begin{array}{l}CH_2.OH\\ |\\ CH.OH\\ |\\ CH_2.OH\end{array}}\longrightarrow\underset{\text{Acrolein.}}{\begin{array}{l}CH_2\\ \|\\ CH\\ |\\ CHO.\end{array}}+2H_2O$$

Acrolein is a volatile liquid with a penetrating and disagreeable odour resembling that of scorched fat. Its vapour is strongly lachrymatory.

Like other aldehydes it reduces ammoniacal silver hydroxide, being itself oxidised to acrylic acid (p. 257):

$$CH_2:CH.CHO\longrightarrow CH_2:CH.COOH.$$

CHAPTER XXIV

THE POLYBASIC CARBOXYLIC ACIDS

OXALIC ACID, $\begin{array}{l}COOH\\ |\\ COOH\end{array}$

OXALIC acid is the simplest of the dibasic carboxylic acids. Its molecular formula is $C_2H_2O_4$, and its formation from glycol (p. 269) shows that its molecule consists of two —COOH groups joined together. In the form of its calcium and acid potassium salts it occurs in many plants, notably in wood sorrel and in rhubarb. Rhubarb rhizome contains, on the average, some 7 per cent of calcium oxalate.

Preparation.—(1) Oxalic acid can be synthesised, in the form of its sodium salt, by heating sodium formate, or by passing carbon dioxide over heated sodium :

$$2H.COONa = \underset{\text{Sodium oxalate.}}{COONa.COONa} + H_2,$$

$$2CO_2 + 2Na = COONa.COONa.$$

(2) In the laboratory oxalic acid is prepared by the action of nitric acid on sucrose (p. 319). A mixture of sucrose with about eight times its weight of concentrated nitric acid is gently warmed in a large flask. A vigorous reaction soon sets in, and copious brown fumes are evolved. If the oxidation becomes too violent the flask must be cooled. When the reaction is at an end the liquid is allowed to stand for several hours, and the crystals of oxalic acid which have been deposited are then separated by filtration, and purified by recrystallisation from water.

(3) On the large scale, oxalic acid is manufactured from sawdust. The sawdust is heated with caustic soda in open iron vessels, when complex changes take place, resulting in the formation of sodium oxalate. The product is extracted with hot water, and the liquor boiled with milk of lime in order to precipitate insoluble calcium oxalate. The precipitate is collected, washed, and treated with the theoretical quantity of dilute sulphuric acid :

$$\begin{array}{l}COO\\ |\\ COO\end{array}\!\!>Ca + H_2SO_4 = \begin{array}{l}COOH\\ |\\ COOH\end{array} + CaSO_4$$

The liquid is filtered from the insoluble calcium sulphate, and the filtrate is evaporated sufficiently for the oxalic acid to crystallise out on cooling.

Commercial oxalic acid, prepared in this way, generally contains sodium oxalate as impurity. For use in volumetric analysis, pure oxalic acid is best prepared by Method (2) from pure sucrose.

Properties.—Oxalic acid forms large colourless crystals containing 2 molecules of water of crystallisation. It is readily soluble in water, has an acid taste, and is poisonous. The crystals melt at 100°. The anhydrous acid, a white amorphous powder, can be obtained by drying at 115°-120°, but at higher temperatures it partly sublimes and partly decomposes, thus :

$$COOH.COOH = CO_2 + CO + H_2O.$$

This decomposition can also be brought about by heating oxalic acid with concentrated sulphuric acid.

Potassium permanganate, in acid solution, oxidises oxalic acid to carbon dioxide and water, and on this reaction depends the use of oxalic acid for standardising permanganate solutions :

$$COOH.COOH + O = 2CO_2 + H_2O.$$

Oxalic acid is a stronger acid than acetic. Its aqueous solution is acid to indicators, and dissolves metallic oxides, hydroxides, and carbonates with formation of salts. Since it is dibasic, oxalic acid gives rise to two series of salts—the normal and the acid oxalates.

Salts and Esters of Oxalic Acid.—Normal potassium oxalate, $COOK.COOK, H_2O$, is prepared by mixing solutions of oxalic acid and potassium carbonate in molecular proportions, and concentrating to crystallisation. If twice the quantity of oxalic acid be employed, potassium hydrogen oxalate, $COOH.COOK$, is formed. Salt of Lemon, or Salt of Sorrel, is crystalline potassium hydrogen oxalate, $COOH.COOK, 2H_2O$. It is sometimes sold mixed with either potassium quadroxalate, $KHC_2O_4.H_2C_2O_4,2H_2O$, or with acid potassium tartrate (p. 68). Ammonium oxalate, $COONH_4.COONH_4,H_2O$, is prepared by neutralising oxalic acid solution with ammonium hydroxide. When heated it yields *oxamide* (compare p. 248) :

$$\begin{array}{l} COONH_4 \\ | \\ COONH_4 \end{array} = \begin{array}{l} CO.NH_2 \\ | \\ CO.NH_2 \end{array} + H_2O.$$

Oxamide.

Calcium oxalate is insoluble in water, and is formed as a white precipitate when a solution of a calcium salt is added to a neutral solution of an oxalate.

Oxalic acid is easily esterified. Methyl oxalate, $COOCH_3.COOCH_3$, is a crystalline solid, melting at 54°, and is prepared by boiling anhydrous oxalic acid with methyl alcohol. It is rapidly hydrolysed by dilute alkalies, and even by hot water.

Ethyl oxalate is a liquid, boiling at 186°.

Tests for Oxalates.—(1) When heated alone, oxalates decompose, with little or no charring, but with evolution of oxides of carbon, leaving a residue of the oxide or carbonate of the metal.

(2) When heated with concentrated sulphuric acid, oxalates are decomposed with evolution of a mixture of carbon monoxide and carbon dioxide, no charring taking place (distinction from tartrate and citrate). The carbon dioxide can be recognised by its action on lime water, and, if sufficient of the oxalate is used to maintain a brisk effervescence, the carbon monoxide can be made to burn at the mouth of the tube.

(3) Calcium chloride, added to a neutral solution of an oxalate, produces a white, crystalline precipitate of calcium oxalate. The precipitate is insoluble in acetic acid (distinction from tartrate and citrate), but dissolves in dilute hydrochloric acid.

MALONIC ACID, $CH_2\Big\langle\begin{array}{l}COOH\\COOH\end{array}$

Malonic acid is the first homologue of oxalic acid. It can be prepared by heating the potassium salt of monochloracetic acid with solid potassium cyanide, and then hydrolysing the product by boiling it with hydrochloric acid :

$$\underset{\text{Potassium chloracetate.}}{CH_2Cl.COOK} + KCN = \underset{\text{Potassium cyano-acetate.}}{CH_2(CN).COOK} + KCl,$$

$$CH_2(CN).COOK + 2HCl + 2H_2O = \underset{\text{Malonic acid.}}{CH_2(COOH)_2} + KCl + NH_4Cl.$$

Malonic acid is a crystalline solid, which, on heating, decomposes into acetic acid and carbon dioxide :

$$CH_2(COOH)_2 = CH_3.COOH + CO_2.$$

SUCCINIC ACID, $\begin{array}{l}CH_2.COOH\\|\\CH_2.COOH\end{array}$

Succinic acid may be obtained by destructive distillation of amber. It can be prepared synthetically by heating ethylene dibromide with solid potassium cyanide, and then hydrolysing the product by boiling with a dilute mineral acid :

$$\begin{array}{l}CH_2Br\\|\\CH_2Br\end{array} \xrightarrow[+2KCN]{} \underset{\text{Ethylene dicyanide.}}{\begin{array}{l}CH_2.CN\\|\\CH_2.CN\end{array}} \xrightarrow[\text{Hydrolysis}]{} \begin{array}{l}CH_2.COOH\\|\\CH_2.COOH.\end{array}$$

Succinic acid is a colourless crystalline solid, melting at 185°,

and is sparingly soluble in water. Like oxalic acid, it is dibasic, and forms both normal and acid salts.

When succinic acid is distilled, it is partially converted into *succinic anhydride*, with loss of water :

$$\begin{array}{l} CH_2.COOH \\ | \\ CH_2.COOH \end{array} \longrightarrow \begin{array}{l} CH_2.CO \\ | \\ CH_2.CO \end{array}\!\!>O + H_2O.$$

Succinic anhydride.

This compound is called an " inner anhydride ", since it is formed from *one* molecule of the acid by what may be termed a process of internal condensation. In this way it differs from, say, acetic anhydride, which is formed by the condensation of *two* molecules of acetic acid (compare p. 250). By heating in a stream of ammonia gas, succinic anhydride can be converted into a compound called *succinimide* :

$$\begin{array}{l} CH_2.CO \\ | \\ CH_2.CO \end{array}\!\!>O + NH_3 = \begin{array}{l} CH_2.CO \\ | \\ CH_2.CO \end{array}\!\!>NH + H_2O.$$

Succinimide.

Succinamide is prepared by shaking ethyl succinate with a strong solution of ammonium hydroxide :

$$\begin{array}{l} CH_2.COOC_2H_5 \\ | \\ CH_2.COOC_2H_5 \end{array} + 2NH_3 = \begin{array}{l} CH_2.CO.NH_2 \\ | \\ CH_2.CO.NH_2 \end{array} + 2C_2H_5.OH.$$

Succinamide.

It cannot, however, be prepared by distilling ammonium succinate, a method which would be analogous to that generally employed for the preparation of acetamide (p. 251), since, at the temperature employed, the succinamide first formed is converted into the imide :

$$\begin{array}{l} CH_2.CO.NH_2 \\ | \\ CH_2.CO.NH_2 \end{array} \longrightarrow \begin{array}{l} CH_2.CO \\ | \\ CH_2.CO \end{array}\!\!>NH + NH_3.$$

MALIC ACID, $\begin{array}{l} CH(OH).COOH \\ | \\ CH_2.COOH \end{array}$

Malic, or hydroxy-succinic acid, occurs in the juice of apples and of other fruits. It can be made synthetically from succinic acid, which, by treatment with bromine, is converted into bromo-succinic acid ; this, on boiling with silver hydroxide and water, yields malic acid :

$$\begin{array}{l} CH_2.COOH \\ | \\ CH_2.COOH \end{array} \longrightarrow \begin{array}{l} CHBr.COOH \\ | \\ CH_2.COOH \end{array} \longrightarrow \begin{array}{l} CH(OH).COOH \\ | \\ CH_2.COOH. \end{array}$$

Malic acid is a crystalline compound, which on reduction with hydriodic acid yields succinic acid.

$$\text{Tartaric Acid, } \begin{array}{l} CH(OH).COOH \\ | \\ CH(OH).COOH \end{array}$$

Tartaric acid is a dihydroxy-succinic acid. It is one of the more important "vegetable acids", and occurs in the juice of many fruits, notably the grape.

Preparation.—(1) Tartaric acid can be prepared synthetically by a method very similar to that given for malic acid. Succinic acid, by the prolonged action of bromine, is converted into symmetrical dibromosuccinic acid, and this, on boiling with silver hydroxide and water, yields tartaric acid:

$$\begin{array}{l} CH_2.COOH \\ | \\ CH_2.COOH \end{array} \longrightarrow \begin{array}{l} CHBr.COOH \\ | \\ CHBr.COOH \end{array} \longrightarrow \begin{array}{l} CH(OH).COOH \\ | \\ CH(OH).COOH. \end{array}$$

(2) During the manufacture of wines by the fermentation of grape juice, a brownish solid called "argol" separates. Argol is impure potassium hydrogen tartrate, and from it the tartaric acid of commerce is obtained.

The argol, after recrystallisation from water, is dissolved in hot water, and chalk is added, small quantities at a time, until effervescence ceases. In this way half the tartaric acid is precipitated as sparingly soluble calcium tartrate, and the rest remains in solution as normal potassium tartrate:

$$2\begin{array}{l} CH(OH).COOK \\ | \\ CH(OH)COOH \end{array} + CaCO_3$$

$$= \begin{array}{l} CH(OH).COO \\ | \\ CH(OH).COO \end{array}\!\!>\!Ca + \begin{array}{l} CH(OH).COOK \\ | \\ CH(OH).COOK \end{array} + CO_2 + H_2O$$

The calcium tartrate is filtered off, and calcium chloride is added to the filtrate, when the remainder of the tartaric acid is precipitated as calcium tartrate:

$$\begin{array}{l} CH(OH).COOK \\ | \\ CH(OH).COOK \end{array} + CaCl_2 = \begin{array}{l} CH(OH).COO \\ | \\ CH(OH).COO \end{array}\!\!>\!Ca + 2KCl.$$

The whole of the calcium tartrate is then treated with the theoretical quantity of dilute sulphuric acid:

$$\begin{array}{l} CH(OH).COO \\ | \\ CH(OH).COO \end{array}\!\!>\!Ca + H_2SO_4 = \begin{array}{l} CH(OH).COOH \\ | \\ CH(OH).COOH \end{array} + CaSO_4.$$

After filtering off the calcium sulphate, the clear solution of tartaric acid is evaporated to crystallisation.

Properties.—Tartaric acid crystallises in large colourless prisms, melting at 167°, with decomposition. It is very easily soluble in water, somewhat less soluble in alcohol, and insoluble in ether.

When heated, it first melts and then chars, giving an odour of burnt sugar. It also chars when gently warmed with concentrated sulphuric acid, and at the same time sulphur dioxide is evolved, owing to the reduction of some of the sulphuric acid.

Salts of Tartaric Acid.—Being a dibasic acid, tartaric acid forms two series of salts. Potassium hydrogen tartrate, $KHC_4H_4O_6$, unlike most potassium salts, is only sparingly soluble in water, and its formation is therefore sometimes used as a test for potassium. Normal potassium tartrate, $(K_2C_4H_4O_6)_2,H_2O$, is readily soluble. Calcium tartrate, $CaC_4H_4O_6,4H_2O$, is only very sparingly soluble in water, and is formed as a white precipitate when a solution of a calcium salt is added to a neutral solution of a tartrate. Many tartrates are important pharmaceutical substances. The following are official, and have been previously described in detail:

Antimonium Tartaratum, $(KSbOC_4H_4O_6)_2,H_2O$ (p. 150).
Potassii Tartras, $(K_2C_4H_4O_6)_2,H_2O$ (p. 67).
Potassii Tartras Acidus, $KHC_4H_4O_6$ (p. 68).
Sodii et Potassii Tartras, $NaKC_4H_4O_6,4H_2O$ (p. 84).
Ferri et Potassii Tartras (p. 136).

Tests for Tartrates.—(1) When heated alone a tartrate chars, giving an odour of burnt sugar.

(2) With concentrated sulphuric acid, tartrates char readily on gentle warming (distinction from oxalates and citrates).

(3) When calcium chloride is added to a neutral solution of a tartrate, a white crystalline precipitate of calcium tartrate is formed, either immediately or on shaking (distinction from citrate). The precipitate is soluble in dilute mineral acids, and also in acetic acid (distinction from oxalate).

ACIDUM TARTARICUM

Tartaric Acid, $H_2C_4H_4O_6$. (Mol. Wt. = 150)

The official substance is required to contain not less than 99 per cent of $H_2C_4H_4O_6$.

It is met with in colourless monoclinic prisms, soluble more than 1-1 in water and 1-3 in alcohol (90 per cent), the aqueous solution being dextro-rotatory (p. 293).

Tests for Impurities. *Non-volatile Matter.*—On strong ignition in an open crucible, it should not leave more than 0·1 per cent of ash.

Copper.—Dissolve in dilute nitric acid, add excess of ammonium hydroxide, and filter if necessary. The solution should have no

blue tinge, and should not become brown on acidifying with acetic acid and adding potassium ferrocyanide.

Iron.—The solution in dilute nitric acid should give no blue or green precipitate or coloration when treated with a solution of potassium ferrocyanide.

Calcium.—Ignite the acid, extract the residue with dilute hydrochloric acid, add excess of ammonium hydroxide, and filter. Add ammonium oxalate to the filtrate, when there should be no immediate precipitate.

Sulphate (*Limit of*).—1 gramme dissolved in 50 mils of water, on addition of 0·5 mil of a 10 per cent solution of barium chloride, should not yield a greater opalescence than 1 mil of N/100 sulphuric acid when precipitated under the same conditions.

Oxalate.—Dissolve in water, treat the solution with dilute acetic acid, and add calcium chloride solution. There should be no white precipitate, even on standing.

Lead Limit.—20 parts per million (p. 173).

Arsenic Limit.—1·4 parts per million (p. 176).

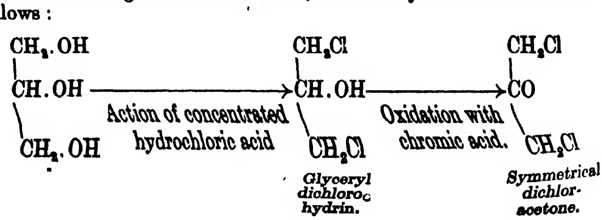
Quantitative Estimation.—It is estimated by neutralisation with standard sodium hydroxide. Weigh out about 5 grammes, dissolve in water, dilute to 100 mils, and titrate portions of 20 mils with N/1 sodium hydroxide, using phenolphthalein as indicator:

$$2NaOH + H_2C_4H_4O_6 = Na_2C_4H_4O_6 + 2H_2O,$$
$$2 \times 40 \equiv 150,$$
$$1000 \text{ mils N/1 NaOH} \equiv 75 \text{ grammes of } H_2C_4H_4O_6,$$
$$1 \text{ mil N/1 NaOH} \equiv 0{\cdot}075 \text{ gramme of } H_2C_4H_4O_6.$$

$CH_2.COOH$
|
CITRIC ACID, $C(OH).COOH$
|
$CH_2.COOH$

Citric acid occurs in large quantities in the juice of various species of *Citrus*, and to a smaller extent in the unripe juices of many fruits. Succus Limonis contains between 7 and 9 per cent of citric acid.

Preparation.—(1) Citric acid can be synthesised from glycerin by an interesting series of reactions, which may be summarised as follows:



$$\xrightarrow[\text{of HCN}]{\text{Direct combination}} \begin{array}{l} CH_2Cl \\ | \\ C(OH).CN \\ | \\ CH_2Cl \end{array} \xrightarrow[\text{dil. mineral acid}]{\text{Hydrolysis with}} \begin{array}{l} CH_2Cl \\ | \\ C(OH).COOH \\ | \\ CH_2Cl. \end{array}$$

Cyanohydrin of symm. dichloracetone.

$$\xrightarrow[\text{potassium salt}]{\text{Action of KCN on}} \begin{array}{l} CH_2.CN \\ | \\ C(OH).COOK \\ | \\ CH_2.CN \end{array} \xrightarrow[\text{with dil. HCl}]{\text{Hydrolysis}} \begin{array}{l} CH_2.COOH \\ | \\ C(OH).COOH \\ | \\ CH_2.COOH. \end{array}$$

(2) Citric acid is manufactured from lemon juice. The boiled juice, after filtration, is neutralised with chalk. The precipitated calcium citrate is separated from the hot solution by filtration, and free citric acid is obtained from it by an exactly similar method to that described for tartaric acid (p. 288).

Properties.—Citric acid forms large colourless crystals, which contain 1 molecule of water of crystallisation, and melt at 100°. It has a pleasant, sour taste. With concentrated sulphuric acid it chars on boiling.

When heated alone it gives off very irritating vapours, with some charring. Under carefully regulated conditions, a number of interesting unsaturated compounds can be obtained from citric acid by the action of heat. Thus if the anhydrous acid is carefully heated at about 170° it is converted into aconitic acid, but if rapidly distilled it yields citraconic acid and its anhydride as the main products :

$$\begin{array}{l} CH_2.COOH \\ | \\ C(OH).COOH \\ | \\ CH_2.COOH \end{array} \rightarrow \begin{array}{l} CH.COOH \\ \| \\ C.COOH \\ | \\ CH_2.COOH \end{array} \longrightarrow \begin{array}{l} CH.COOH \\ \| \\ C.COOH \\ | \\ CH_3 \end{array} \longrightarrow \begin{array}{l} CH.CO \\ \| \\ C.CO \\ | \\ CH_3 \end{array}\!\!\Big\rangle O.$$

Aconitic acid. Citraconic acid. Citraconic anhydride.

Salts of Citric Acid.—Citric acid is tribasic, and forms three series of salts. Calcium citrate, $(C_6H_5O_7)_2Ca_3$, has the unusual property of being fairly soluble in cold water, but only sparingly soluble in hot. The following official citrates have been described :

Liquor Ammonii Citratis (p. 96).
Liquor Bismuthi et Ammonii Citratis (p. 154).
Ferri et Ammonii Citras (p. 133).
Ferri et Quininæ Citras (p. 135).
Lithii Citras, $Li_3C_6H_5O_7,4H_2O$ (p. 89).
Potassii Citras, $K_3C_6H_5O_7,H_2O$ (p. 68).

Tests for Citrates.—(1) When heated alone citrates char, giving an unpleasant odour.

(2) With concentrated sulphuric acid, citrates do not char in the cold or on gentle warming (distinction from tartrate). On continued heating the liquid gradually darkens in colour until, on boiling, it becomes nearly black (distinction from oxalate).

(3) When a neutral solution of a citrate is shaken in the cold with calcium chloride no precipitation takes place. On boiling for a minute or two, a white crystalline precipitate of calcium citrate is formed (distinction from tartrate and oxalate).

ACIDUM CITRICUM

Citric Acid, $H_3C_6H_5O_7,H_2O$. (Mol. Wt. = 210)

The official substance is required to contain not less than 99·5 per cent of $H_3C_6H_5O_7,H_2O$.

It is met with in the form of large colourless prisms. Soluble about 1 in 0·5 in water, somewhat less soluble in alcohol (90 per cent), slightly soluble in ether.

Tests for Impurities. *Non-volatile Matter.*—On strong ignition in an open crucible, it should leave not more than 0·05 per cent of ash.

Iron.—The aqueous solution, acidified with dilute nitric acid, should give no blue or green precipitate or coloration when treated with a solution of potassium ferrocyanide.

Calcium.—No immediate precipitate should be produced when the acid is ignited and tested as under Acidum Tartaricum.

Sulphate.—The aqueous solution, acidified with dilute hydrochloric acid, should give no more than a slight turbidity with barium chloride.

Tartaric Acid.—This test depends on the previously mentioned fact that tartaric acid chars more readily with concentrated sulphuric acid than does citric acid. 1 gramme of the powdered citric acid is mixed in a test tube with 10 mils of concentrated sulphuric acid, and the tube is heated on a water-bath at 90° for an hour. Not more than a pale yellow colour should be developed.

Lead Limit.—20 parts per million (p. 173).

Arsenic Limit.—1·4 parts per million (p. 176).

Quantitative Estimation.—Citric acid is estimated in a manner exactly similar to that described under Acidum Tartaricum, using the same quantities :

$$3NaOH + H_3C_6H_5O_7 = Na_3C_6H_5O_7 + 3H_2O,$$
$$3 \times 40 \equiv 210,$$
$$1000 \text{ mils } N/1 \text{ NaOH} \equiv 70 \text{ grammes of } H_3C_6H_5O_7,H_2O,$$
$$1 \text{ mil } N/1 \text{ NaOH} \equiv 0{\cdot}070 \text{ gramme of } H_3C_6H_5O_7,H_2O.$$

CHAPTER XXV

STEREOISOMERISM

Optical Isomerism

In the study of organic chemistry certain examples of isomerism are met with which cannot be explained by ordinary structural formulæ. One of the simplest cases is that of the lactic acids. In addition to ordinary lactic acid (p. 253) an isomeric compound occurs in meat juices, known as *sarco-lactic acid,* which is identical with the ordinary acid in chemical properties, but differs from it in certain minor physical properties, notably in its effect on polarised light.

For a full account of the nature of polarised light the student must be referred to text-books of physics, and only the essential facts can be mentioned here. Modern physical theory supposes that the phenomena of light are due to the propagation through the ether of a series of waves or vibrations. In a parallel beam of light the vibrations take place indiscriminately, in all planes passing through the line of direction of the beam. By passing a beam of light through certain transparent crystalline substances, such as tourmaline, it is possible to cut out all the vibrations except those in one plane, and in this way there is produced what is known as a beam of polarised light.

Certain substances, either in the free state or in solution, are capable, when interposed in the path of a beam of polarised light, of rotating the plane of polarisation, either to the right (dextro) or to the left (lævo).[1] Such substances are said to be "optically active". The amount of rotation produced by a particular substance can be expressed, for purposes of comparison, as a definite numerical property—the *specific rotation*—for the determination of which an instrument called a polarimeter is employed.

Ordinary lactic acid is optically inactive, whereas sarco-lactic acid is dextro-rotatory. Since the two forms are identical in chemical properties, they must necessarily be both represented by the same structural formula, namely, $CH_3.CH(OH).COOH$. Now hundreds of optically active organic compounds are known, and an inspection of the structural formulæ of such compounds

[1] The words *dextro* and *lævo* are often abbreviated to *d* and *l* respectively.

reveals the interesting fact that in every case the molecule contains at least one carbon atom which is directly attached to four dissimilar atoms or groups, and which is therefore said to be asymmetric. The following compounds, for example, are all optically active, and each contains one or more asymmetric carbon atoms (shown in heavy type):

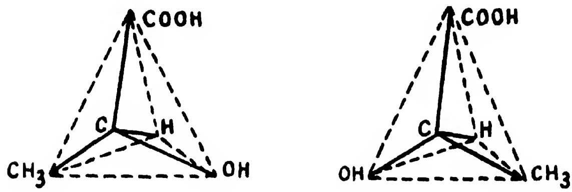
$CH_3.\mathbf{C}H(OH).COOH$	Lactic acid.
$\begin{array}{l} CH_2.COOH \\ \vert \\ \mathbf{C}H(OH).COOH \end{array}$	Malic acid.
$\begin{array}{l} \mathbf{C}H(OH).COOH \\ \vert \\ \mathbf{C}H(OH).COOH \end{array}$	Tartaric acid.
$\begin{array}{l} C_2H_5 \\ CH_3 \end{array} \!\!>\! \mathbf{C}H.CH_2.OH$	Optically active amyl alcohol.
$\begin{array}{l} C_2H_5 \\ CH_3 \end{array} \!\!>\! \mathbf{C}H.COOH$	Optically active valerianic acid.

In the case of each of these compounds, an isomeric compound is known which is identical chemically, but rotates the plane of polarisation of light to an exactly equal extent in the opposite direction. Such pairs of compounds are called optical isomerides.

It is evident, then, that the phenomena of optical activity and optical isomerism are intimately connected with the presence in the molecule of an asymmetric carbon atom.[1] This connection was recognised by two scientists, Le Bel and van't Hoff, who put forward independent explanations of optical isomerism; and their views, which are in agreement on main points, are now commonly accepted. Although ordinary structural formulæ necessarily represent the atoms composing a molecule as being all in one plane, there is no reason to suppose that this is actually the case. In methane, for example, the hydrogen atoms may be supposed to be regularly arranged in space around the central carbon atom: or, in other words, a carbon atom may be assumed to lie at the centre of an imaginary regular tetrahedron, the valency bonds being directed towards the corners. This being granted, it will be seen that the molecule of an organic compound should be represented, not by a formula drawn on a plane surface, but by a solid figure; that is, by a spacial or *stereo* formula.

[1] Some optically active compounds are known which owe their activity to an asymmetric atom other than carbon. They are, however, comparatively few in number, and of little importance.

Now, provided that two or more of the groups or atoms attached to a carbon atom are identical, then no matter at which corner of the imaginary tetrahedron each atom or group is placed, the same solid figure results. If, on the other hand, the four atoms or groups are all different, then two arrangements are possible. In the case of lactic acid these two arrangements are :



I II

(I.) and (II.) are not identical solid figures, and cannot be superimposed on one another. They are related as is an object to its image in a mirror, or a right-hand glove to a left-hand glove. Such pairs of objects are known as enantiomorphs. It is assumed that one of these stereo-formulæ represents sarco-lactic acid, and the other a chemically identical compound of equal but opposite optical rotation. Ordinary inactive lactic acid is a mixture of these two stereoisomers in equal proportions. If this be so, it should be possible to separate ordinary lactic acid (the *dl*- mixture) into its two optically active components. This can actually be done, but only with considerable difficulty, since the two active forms are identical, not only in chemical properties, but also in such physical properties as melting-point, boiling-point, and solubility.

Resolution of *dl*- mixtures.—Many naturally occurring compounds containing asymmetric carbon atoms are optically active. When such compounds are made synthetically, starting from compounds containing no asymmetric carbon atom, the product is nearly always optically inactive, since the *d*- and *l*- forms are produced indiscriminately, and consequently in equal proportions. Further, many optically active compounds are readily converted into the inactive *dl*- mixture on heating or under the influence of various reagents, this process being known as racemisation. It is often necessary to separate such *dl*- mixtures into their two components, the process being known as resolution. The more important methods employed in accomplishing this will now be briefly explained.

1. *Mechanical Separation.*—The two components of a solid *dl*- mixture differ slightly in crystalline form, being, in fact, enantiomorphous ; and, provided that the crystals are sufficiently large, it is sometimes possible to pick out the *d*- and the *l*- crystals separately from the mixture. In this way it has been found possible to resolve lactic acid by crystallisation of its zinc ammonium salt, and

racemic acid (p. 297) by crystallisation of its sodium ammonium salt. The method is, however, of very limited application.

2. *Action of Organisms.*—Certain living organisms assimilate and decompose one component of certain *dl*- mixtures, leaving the other component behind. Thus a solution of ordinary ammonium lactate (inactive) is rendered optically active by allowing *Penicillium glaucum* to grow in it, owing to the fact that the mould assimilates the *l*- form more rapidly than the *d*- form. By such methods as this it is, of course, only possible to isolate one component of a *dl*- mixture, since the other is decomposed.

3. *Use of Optically Active Compounds.*—This is a widely used and general method for the resolution of *dl*- acids and bases. If a *dl*- acid, for example, is combined with a *d*- base, two compounds are produced ; the process can be represented as follows :

$$2(d\text{- base}) + (d\text{- acid} + l\text{- acid}) \longrightarrow d\text{- base}\,.\,d\text{- acid} + d\text{- base}\,.\,l\text{- acid}.$$

The two compounds on the right-hand side of the "equation" are not enantiomorphous ; unlike enantiomorphs, they differ from one another in melting-point, boiling-point, solubility, and other physical properties, so that, as a general rule, it is possible to separate them by the ordinary methods of fractional crystallisation or distillation. Once this has been done it is only necessary to hydrolyse the two products, when one yields the *d*- and the other the *l*- form of the original *dl*- acid. A *dl*- base can be resolved in a similar manner by combining it with an optically active acid.

dl- Lactic acid has been resolved by this method, by fractional crystallisation of its strychnine salt.

Isomerism of the Tartaric Acids.—An inspection of the structural formula of tartaric acid (p. 288) will show that the molecule contains two asymmetric carbon atoms. By the aid of solid models it can be shown that such a molecule can exist, theoretically, in three different stereo-forms. These forms may be conveniently represented as plane projections, thus :

$$\begin{array}{ccc}
\begin{array}{c} \mathrm{COOH} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{COOH.} \end{array} &
\begin{array}{c} \mathrm{COOH} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{COOH.} \end{array} &
\begin{array}{c} \mathrm{COOH} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{COOH.} \end{array} \\
\text{I.} & \text{II.} & \text{III.}
\end{array}$$

These are what may be termed *configurational formulæ*, since they attempt to show, not only the way in which the atoms are linked together, but also the actual configuration of the molecule, that is, the arrangement of the atoms in space.

Formulæ I. and II. are enantiomorphously related, and it may

be assumed that they represent respectively a *d-* and an *l-* form of tartaric acid. A mixture of the two in equal proportions would constitute an optically inactive *dl-* mixture.

Formula III. represents a molecule which, although containing two asymmetric carbon atoms, has a plane of symmetry, and would therefore be optically inactive. In other words, it may be said that the optical rotational effect of one asymmetric carbon atom is counterbalanced by the opposite effect of the other; so that the molecule is optically inactive by "internal compensation", as distinguished from the *dl-* mixture of I. and II., which is inactive by "external compensation".

All these forms of tartaric acid actually exist, and in addition there is known a substance called *racemic acid*, which is simply a definite crystallographic compound of the *d-* and *l-* forms, as distinguished from the mere *dl-* mixture, in which each component retains its own crystallographic identity.

d- Tartaric acid (Formula I.) is the ordinary tartaric acid of the Pharmacopœia, and has been previously described (p. 289).

l- Tartaric acid (Formula II.) has been made by resolution of racemic acid (see below). It is identical with the *d-* form in chemical and physical properties, except that it rotates the plane of polarisation to an equal extent to the left, and that its crystalline form is slightly different.

Racemic acid is the product actually obtained when symmetrical dibromosuccinic acid is heated with silver hydroxide and water. It differs from the *d-* and *l-* acids in crystalline form, solubility, and other physical properties.

Racemic acid has been resolved by Pasteur by the following method: Sodium ammonium racemate, $Na(NH_4)C_4H_4O_6, 2H_2O$, can be easily prepared by mixing solutions of racemic acid, sodium hydroxide, and ammonium hydroxide, and crystallising the salt from the hot solution. It is a crystalline solid, which differs in physical properties from both *d-* and *l-* sodium ammonium tartrates. If, however, a solution of sodium ammonium racemate is allowed to crystallise below 27°, the product consists, not of the racemate, but of a mixture of *d-* and *l-* sodium ammonium tartrates, the crystals of which are deposited side by side. The two kinds of crystals thus obtained are slightly different, being related as an object to its mirror image; by careful sorting they can be separated, after which *d-* tartaric acid can be liberated from one kind and *l-* tartaric acid from the other.

Mesotartaric acid (Formula III.) is the internally compensated compound, and cannot therefore be resolved into optically active components. It is formed, together with some racemic acid, when ordinary *d-* tartaric acid is heated with water in sealed tubes. It differs considerably from racemic acid and from the two active acids in crystalline form, melting-point, solubility, and other physical properties.

Geometrical Isomerism

In the case of certain unsaturated compounds a form of stereoisomerism is met with which can be best illustrated by a familiar example.

Malic acid (p. 287) can exist in either of two optically active forms, or as a *dl*-mixture. If any of these varieties of malic acid is heated, a mixture of two unsaturated acids, called respectively maleic and fumaric acids, is produced. These two acids are very similar in chemical properties, and their reactions point to the fact that they both have the same structural formula, namely,

$$\begin{array}{l} CH.COOH \\ \| \\ CH.COOH. \end{array}$$

Now maleic and fumaric acids differ widely in physical properties. Their isomerism is of quite a different type from that of optical isomerides, since neither of them is optically inactive, nor do their molecules contain asymmetric carbon atoms. On reduction, they both yield succinic acid, $\begin{array}{l} CH_2.COOH \\ | \\ CH_2.COOH \end{array}$, which only exists in one form, so that the isomerism is evidently connected in some way with the presence of the double bond in the molecule.

It is believed that in the case of a compound like succinic acid, in which the carbon atoms are connected by a single bond, the atoms or groups attached to each carbon atom are free to rotate about the single bond as axis. In the case of maleic or fumaric acid, in which two carbon atoms are joined by a double bond, this free rotation is prevented, so that two stable configurational arrangements are possible, one of which must represent maleic acid and the other fumaric :

$$\begin{array}{ccc} \begin{array}{c} H—C—COOH \\ \| \\ H—C—COOH. \\ \text{I.} \end{array} & \qquad & \begin{array}{c} H—C—COOH \\ \| \\ COOH—C—H. \\ \text{II.} \end{array} \end{array}$$

Now although the two acids are very similar in chemical properties, they differ in one very important respect. On heating, fumaric acid sublimes unchanged, but maleic acid is converted into maleic anhydride, $\begin{array}{l} CH.CO\diagdown \\ |\qquad\quad\ \ >O \\ CH.CO\diagup \end{array}$. This fact is evidence of a close proximity of the —COOH groups in maleic acid, which is therefore represented by Formula I., Formula II. being reserved for fumaric acid.

It should be noted that this type of isomerism is only possible

when two different atoms or groups are attached to each of the carbon atoms joined by the double bond. Thus:

$$\text{ethylene,}\quad \begin{array}{c} H\text{—}C\text{—}H \\ \| \\ H\text{—}C\text{—}H, \end{array} \qquad \text{and propylene,}\quad \begin{array}{l} H\text{—}C\text{—}H \\ \quad\ \| \\ H\text{—}C\text{—}CH_3, \end{array}$$

can exist in only one form, although two symmetrical dimethyl ethylenes,

$$\begin{array}{l} H\text{—}C\text{—}CH_3 \\ \quad\ \| \\ H\text{—}C\text{—}CH_3 \end{array} \qquad \text{and} \qquad \begin{array}{r} H\text{—}C\text{—}CH_3 \\ \| \quad\quad\ \\ CH_3\text{—}C\text{—}H, \end{array}$$

are capable of existence.

CHAPTER XXVI

THE CYANOGEN COMPOUNDS

THE cyanogen compounds, some of which are of considerable importance, contain the univalent cyanogen radicle $—C{\equiv}N$ or $—CN$. This, like the alkyl and other radicles, often passes unchanged through a series of reactions, and in this way behaves very much like a single element. Cyanogen itself, $\begin{matrix}CN\\ |\\ CN\end{matrix}$ or C_2N_2, is not a substance of great importance, but is of theoretical interest, as being the simplest compound of this class.

HYDROCYANIC ACID, HCN

Hydrocyanic acid is fairly widely distributed in Nature, and occurs in combination in many plants, in the form of "cyanogenetic" glucosides, such as amygdalin and prulaurasin (p. 382). These glucosides, on hydrolysis with water in the presence of certain enzymes, yield free hydrocyanic acid. Hydrocyanic acid is present in small quantities in crude coal-gas.

Preparation.—(1) Hydrocyanic acid can be prepared from its elements by strongly heating carbon in an atmosphere of hydrogen and nitrogen:

$$2C + N_2 + H_2 = 2HCN.$$

(2) It is formed when ammonium formate (or formamide) is heated, in presence of phosphorus pentoxide as a dehydrating agent:

$$H.COONH_4 = H.CO.NH_2 + H_2O,$$
$$H.CO.NH_2 = HCN + H_2O.$$

(3) It is liberated when most metallic cyanides are treated with a dilute acid:

$$KCN + HCl = KCl + HCN.$$

(4) In the laboratory it is prepared by heating potassium ferrocyanide with dilute sulphuric acid: [1]

$$2K_4Fe(CN)_6 + 3H_2SO_4 = FeK_2Fe(CN)_6 + 3K_2SO_4 + 6HCN.$$

[1] Cf. p. 306.

The mixture is gently heated in a retort connected by means of an efficient condenser to a receiver cooled in ice. The distillate consists of a mixture of hydrocyanic acid and water, from which the pure acid can be obtained by fractional distillation and dehydration over anhydrous calcium chloride.

Properties.—Anhydrous hydrocyanic acid is a colourless, very volatile liquid, which boils at 25°, is miscible with water, and has an odour resembling that of crushed bitter almonds. Being very poisonous, the anhydrous acid is dangerous to handle, and it is therefore usually met with in the form of dilute aqueous solutions.

Hydrocyanic acid is rapidly hydrolysed by hot dilute mineral acids, with production of ammonium formate:

$$HCN + 2H_2O = H.COONH_4.$$

This hydrolysis takes place slowly when an aqueous solution of the acid is kept for a long time.

Hydrocyanic acid is a very feeble acid. Its solutions turn blue litmus a dull claret colour, and its salts are decomposed by mineral acids, and even by carbonic acid. For example:

$$KCN + H_2O + CO_2 = HCN + KHCO_3.$$

For this reason most metallic cyanides develop a strong odour of hydrocyanic acid on exposure to air.

Hydrocyanic acid is generally believed to have the structure $H-C \equiv N$, or $H.C \vdots N$, the hydrogen and nitrogen atoms being both directly linked to the carbon atom.

ACIDUM HYDROCYANICUM DILUTUM

Diluted Hydrocyanic Acid, HCN. (Mol. Wt. = 27.)
Syn. Dilute Prussic Acid

This is an aqueous solution containing 2 per cent by weight of HCN, and having a specific gravity of 0·997. It is prepared by distilling a mixture of potassium ferrocyanide with dilute sulphuric acid, and diluting the distillate to the required strength. It should be stored in a dark place, in small, inverted-stoppered bottles of amber-coloured glass.[1]

Tests for Impurities. *Insoluble Matter.*—5 mils, evaporated in a platinum dish (in a fume-cupboard), should leave no appreciable residue.

Other Acids.—It should be only slightly acid to litmus.

Sulphate.—Add hydrochloric acid and barium chloride. There should be no more than a faint turbidity.

Chloride.—Boil in a fume-cupboard with an efficient draught until the hydrocyanic acid is expelled. Add nitric acid and silver nitrate, when there should be not more than a slight opalescence.

[1] Scheele's Prussic Acid, sometimes met with in commerce, contains 4 per cent of HCN.

Quantitative Estimation.—*If a little silver nitrate be added to a solution of potassium cyanide, the precipitate of silver cyanide first formed dissolves in the excess of potassium cyanide to form a soluble double salt*:

$$(i.)\ AgNO_3 + KCN = AgCN + KNO_3,$$
$$(ii.)\ AgCN + KCN = AgCN,KCN.$$

When all the cyanide has been converted into the double salt, the further addition of silver nitrate produces a permanent precipitate of silver cyanide:

$$(iii.)\ AgCN,KCN + AgNO_3 = 2AgCN + KNO_3.$$

If, therefore, a solution of potassium cyanide be titrated with standard silver nitrate, a permanent precipitate is first formed when the reactions represented by equations (i.) and (ii.) are complete.

Diluted hydrocyanic acid can be estimated by adding excess of potassium or sodium hydroxide, and titrating the resulting solution of potassium or sodium cyanide with standard silver nitrate. It is, however, more usual to employ ammonium hydroxide for rendering the solution alkaline. In this case, owing to the solubility of silver cyanide in ammonium hydroxide, a little potassium iodide must be employed as indicator, the end-point being indicated by the first appearance of a precipitate of silver iodide.

Measure 5 mils of diluted hydrocyanic acid from a burette, dilute to about 50 mils, and add about 5 mils of 10 per cent ammonium hydroxide and a few drops of potassium iodide solution. Titrate slowly with N/10 silver nitrate until a permanent opalescence is produced (this can be best observed by placing a piece of black paper under the titration flask):

$$AgNO_3 + 2NH_4CN = AgCN,NH_4CN + NH_4NO_3,$$
$$AgNO_3 \equiv 2NH_4CN \equiv 2HCN,$$
$$170 \equiv 54,$$
$$1000 \text{ mils N/1 } AgNO_3 \equiv 54 \text{ grammes of HCN},$$
$$1 \text{ mil N/10 } AgNO_3 \equiv 0{\cdot}0054 \text{ gramme of HCN}.$$

Aqua Laurocerasi (p. 3) is estimated in the same way. Take 60 mils for each titration.

The Cyanides

Potassium cyanide, KCN, can be prepared by passing the vapour of anhydrous hydrocyanic acid into alcoholic potash. The potassium cyanide, being insoluble in alcohol, is deposited in crystals:

$$KOH + HCN = KCN + H_2O.$$

It is manufactured by strongly heating potassium ferrocyanide out of contact with air, and by other methods:

$$K_4Fe(CN)_6 = FeC_2 + 4KCN + N_2.$$

Potassium cyanide is generally met with in the form of white crystalline lumps, which on exposure to air develop a strong odour of hydrocyanic acid. It is easily soluble in water, forming an alkaline solution, and is very poisonous. Dilute mineral acids decompose it, with evolution of hydrocyanic acid:

$$2KCN + H_2SO_4 = 2HCN + K_2SO_4.$$

Fused potassium cyanide is a powerful reducing agent, and readily takes up an atom of oxygen to form potassium cyanate, KOCN. For this reason it is sometimes employed in qualitative analysis to assist the formation of metallic beads by heating metallic oxides on charcoal:

$$KCN + PbO = KOCN + Pb.$$

Solutions of potassium cyanide are employed for the extraction of gold from its ores.

Silver cyanide, AgCN, is formed as a white precipitate when silver nitrate is added to a solution of potassium cyanide. It is readily soluble in ammonium hydroxide, but is insoluble in dilute acids. Concentrated nitric acid slowly dissolves it on boiling.

When strongly heated, silver cyanide is decomposed into metallic silver and *cyanogen*, C_2N_2:

$$2AgCN = 2Ag + C_2N_2.$$

Cyanogen is a colourless, poisonous gas, with an odour recalling that of hydrocyanic acid. It burns with a peach-coloured flame, with formation of carbon dioxide and nitrogen:

$$C_2N_2 + 2O_2 = 2CO_2 + N_2.$$

Mercuric cyanide, $Hg(CN)_2$, is prepared by dissolving mercuric oxide in dilute hydrocyanic acid:

$$HgO + 2HCN = Hg(CN)_2 + H_2O.$$

It is a colourless crystalline compound, which, like silver cyanide, decomposes on heating with evolution of cyanogen:

$$Hg(CN)_2 = Hg + C_2N_2.$$

Mercuric cyanide is peculiar in that its aqueous solutions give no precipitate of mercuric iodide on addition of potassium iodide, or of silver cyanide on addition of silver nitrate.

The **alkyl cyanides**, or *nitriles*, are compounds of considerable theoretical interest. They are formed when the ammonium salts or amides of the fatty acids are distilled with phosphorus pentoxide; for example:

$$CH_3.COONH_4 = CH_3.CO.NH_2 + H_2O,$$
$$CH_3.CO.NH_2 = \underset{\substack{\text{Methyl}\\ \text{cyanide.}}}{CH_3.CN} + H_2O.$$

They can also be prepared by heating the alkyl halogen compounds with potassium cyanide :

$$C_2H_5Br + KCN = C_2H_5.CN + KBr.$$

The alkyl cyanides are colourless liquids. They are readily hydrolysed by boiling dilute alkalies, with evolution of ammonia and formation of a salt of the corresponding fatty acid :

$$CH_3.CN + KOH + H_2O = CH_3.COOK + NH_3.$$

On reduction, they yield primary amines (p. 309) :

$$C_2H_5.CN + 4H = \underset{\text{Propylamine.}}{C_2H_5.CH_2.NH_2}.$$

The *alkyl isocyanides* or *isonitriles*, sometimes known as *carbylamines*, are isomeric with the nitriles. They are formed when a primary amine is warmed with chloroform and alcoholic potash :

$$CH_3.NH_2 + 3KOH + CHCl_3 = CH_3.N\ C + 3KCl + 3H_2O.$$

The isonitriles are volatile liquids, and have a disgusting odour. They differ from the nitriles in that the alkyl group and the remaining carbon atom are both directly joined to the (quinquevalent) nitrogen atom. This explains the fact that, when boiled with dilute mineral acids, the isonitriles are split up, with formation of formic acid and an amine :

$$CH_3.N.C + 2H_2O = CH_3.NH_2 + H.COOH.$$

Tests for Cyanides.—(1) Most soluble cyanides, on treatment with dilute hydrochloric or sulphuric acid, evolve an odour of hydrocyanic acid.

(2) A solution of a cyanide gives, on addition of excess of silver nitrate, a white precipitate of silver cyanide, insoluble in dilute nitric acid, but readily soluble in ammonium hydroxide. The precipitate slowly dissolves in hot concentrated nitric acid (distinction from chloride).

(3) A solution of a cyanide, when boiled with ferrous sulphate and sodium hydroxide, is converted into a ferrocyanide :

$$Fe(OH)_2 + 6NaCN = Na_4Fe(CN)_6 + 2NaOH.$$

On acidifying the solution with dilute hydrochloric acid and adding a few drops of ferric chloride a precipitate of Prussian blue is produced.

Ferro- and Ferri-cyanides

When potassium cyanide is added to a solution of a ferrous salt a white precipitate of ferrous cyanide is produced :

$$FeSO_4 + 2KCN = K_2SO_4 + Fe(CN)_2.$$

This precipitate is readily soluble in excess of potassium cyanide, with formation of potassium ferrocyanide :

$$Fe(CN)_2 + 4KCN = \underset{\text{Potassium ferrocyanide.}}{K_4Fe(CN)_6}.$$

Potassium ferrocyanide may be regarded as a compound of potassium cyanide and ferrous cyanide, of the formula $4KCN,Fe(CN)_2$. It is not, however, merely a double salt, since it fails to respond to many of the ordinary tests for cyanides or for ferrous salts ; thus, its aqueous solution yields no precipitate of silver cyanide on addition of silver nitrate, and the iron cannot be precipitated by ammonium hydroxide. These and other considerations point to the fact that potassium ferrocyanide is the potassium salt of hydroferrocyanic acid, $H_4Fe(CN)_6$, the Fe atom and the —CN groups being present as part of the complex acidic radicle, $Fe(CN)_6$. Hydroferrocyanic acid itself is precipitated in small colourless needles when concentrated hydrochloric acid is added to a solution of a ferrocyanide :

$$K_4Fe(CN)_6 + 4HCl = \underset{\text{Hydroferro-cyanic acid.}}{H_4Fe(CN)_6} + 4KCl.$$

Certain oxidising agents convert potassium ferrocyanide into potassium ferricyanide, $K_3Fe(CN)_6$. This change may be represented as simply involving the oxidation of the iron from the ferrous to the ferric state :

$$\underset{\text{Potassium ferrocyanide.}}{4KCN,Fe(CN)_2} \longrightarrow \underset{\text{Potassium ferricyanide.}}{3KCN,Fe(CN)_3}.$$

But potassium ferricyanide, like the ferrocyanide, does not give the ordinary reactions of cyanides or of iron salts, and it should be regarded, not as a double salt of the formula $3KCN,Fe(CN)_3$, but as the potassium salt of hydroferricyanic acid, $H_3Fe(CN)_6$.

Potassium Ferrocyanide, $K_4Fe(CN)_6$.—This compound is an important article of commerce. It can be easily and cheaply manufactured, and is therefore employed as the starting substance for the preparation of many other cyanogen compounds.

Potassium ferrocyanide is formed when ferrous hydroxide is boiled with a solution of potassium cyanide, as in the test for nitrogen (p. 190) :

$$Fe(OH)_2 + 6KCN = K_4Fe(CN)_6 + 2KOH.$$

It is manufactured by melting together in iron vessels a mixture of potassium carbonate, iron filings, and nitrogenous organic substances such as hoof-shavings, animal hide, or dried blood. The melt is allowed to cool, extracted with boiling water, filtered, and the filtrate is evaporated and allowed to crystallise.

The changes which occur during these processes are complex. It may be assumed that the potassium carbonate and the iron react with some of the carbon and nitrogen present to form a mixture of potassium cyanide, KCN, and ferrous cyanide, $Fe(CN)_2$. On boiling the product with water, these two cyanides combine to form potassium ferrocyanide :

$$4KCN + Fe(CN)_2 = K_4Fe(CN)_6.$$

Considerable quantities of potassium ferrocyanide are now manufactured from hydrocyanic acid obtained from crude coal-gas.

Potassium ferrocyanide forms yellow crystals, containing 3 molecules of water of crystallisation. It is fairly readily soluble in water. When strongly heated it decomposes, with formation of potassium cyanide and iron carbide :

$$K_4Fe(CN)_6 = 4KCN + FeC_2 + N_2.$$

Potassium ferrocyanide is decomposed by warm sulphuric acid, the course of the reaction depending upon the concentration of the acid. With dilute sulphuric acid hydrocyanic acid is produced :

$$2K_4Fe(CN)_6 + 3H_2SO_4 = \underset{\substack{\text{Ferrous} \\ \text{potassium} \\ \text{ferrocyanide} \\ \text{(Everett's salt).}}}{FeK_2Fe(CN)_6} + 3K_2SO_4 + 6HCN.$$

With the concentrated acid carbon monoxide is evolved :

$$K_4Fe(CN)_6 + 6H_2SO_4 + 6H_2O = 2K_2SO_4 + FeSO_4 + 3(NH_4)_2SO_4 + 6CO.$$

Potassium ferrocyanide gives, with solutions of ferric salts, a deep blue precipitate of "Prussian blue", or ferric ferrocyanide, $Fe_4[Fe(CN)_6]_3$, and with solutions of cupric salts a dark brown precipitate of cupric ferrocyanide, $Cu_2Fe(CN)_6$.

Potassium Ferricyanide, $K_3Fe(CN)_6$.—This compound is made by the oxidation of potassium ferrocyanide. In practice, a solution of the ferrocyanide is saturated with chlorine gas, and the liquid is then evaporated to crystallisation :

$$2K_4Fe(CN)_6 + Cl_2 = 2K_3Fe(CN)_6 + 2KCl.$$

Potassium ferricyanide forms dark, brownish-red crystals, readily soluble in water. It is a fairly powerful oxidising agent, being readily reduced, in alkaline solution, to potassium ferrocyanide.

Potassium ferricyanide gives with solutions of ferrous salts a deep blue precipitate of "Turnbull's blue", which is apparently identical with Prussian blue. In this reaction the potassium ferricyanide probably oxidises the ferrous salt to ferric, being itself reduced to potassium ferrocyanide. The ferric salt and the potassium ferrocyanide then react to form ferric ferrocyanide.

CYANATES AND THIOCYANATES

Potassium cyanate, KOCN, is prepared by fusing potassium cyanide with litharge :

$$KCN + PbO = KOCN + Pb.$$

The product is extracted with dilute alcohol, filtered, and the filtrate evaporated to crystallisation.

Potassium cyanate is a colourless, crystalline compound, and is a salt of the very unstable compound cyanic acid, HOCN. When boiled with water it is hydrolysed to a mixture of potassium and ammonium carbonates :

$$2KOCN + 4H_2O = K_2CO_3 + (NH_4)_2CO_3.$$

Ammonium cyanate, NH_4OCN, is formed, in solution, when solutions of potassium cyanate and an ammonium salt are mixed :

$$2KOCN + (NH_4)_2SO_4 = 2NH_4OCN + K_2SO_4.$$

If the solution is evaporated to dryness the ammonium cyanate is converted almost completely into urea, $CO(NH_2)_2$. This reaction involves simply a rearrangement of the atoms within the molecule, and is therefore an example of intra-molecular isomeric change. Using the commonly accepted constitutional formulæ for ammonium cyanate and urea, it can be represented as follows :

$$\underset{\text{Ammonium cyanate.}}{NH_4.O.C\ N} \longrightarrow \underset{\text{Urea.}}{O{=}C\begin{matrix}\diagup NH_2\\ \diagdown NH_2\end{matrix}}.$$

Potassium thiocyanate, KSCN, or potassium sulphocyanide as it is sometimes called, is the sulphur compound corresponding to potassium cyanate. It is prepared by fusing potassium cyanide with sulphur :

$$KCN + S = KSCN.$$

Ammonium thiocyanate, NH_4SCN, is made by heating carbon disulphide with an alcoholic solution of ammonia :

$$4NH_3 + CS_2 = NH_4SCN + (NH_4)_2S.$$

It forms colourless, deliquescent crystals. When heated for several hours at about 150° it is partially converted into thiourea, $CS(NH_2)_2$, by a process of intra-molecular change which is exactly analogous to the formation of urea from ammonium cyanate :

$$NH_4SCN = CS(NH_2)_2.$$

A solution of a thiocyanate gives, on treatment with a ferric salt, a deep blood-red coloration, due to the formation of ferric thiocyanate, $Fe(SCN)_3$.

Allyl iso-thiocyanate, $CH_2 : CH . CH_2 . N : C : S$, is a constituent of

the glucoside sinigrin (p. 383), which occurs in the seeds of *Brassica sinapoides*. If the seeds are macerated with water the glucoside undergoes hydrolysis, under the influence of the enzyme myrosin, with liberation of the allyl iso-thiocyanate.

Allyl iso-thiocyanate is a colourless liquid, with a pungent and characteristic odour. When brought into contact with the skin it causes blisters.

Estimation of Allyl Iso-thiocyanate in Oleum Sinapis Volatile.—This estimation depends upon the fact that allyl iso-thiocyanate combines directly with ammonia to form *thiosinamine*, $C_3H_5.NH.CS.NH_2$, which reacts with silver nitrate, in alcoholic ammoniacal solution, to form *allyl cyanamide*, $C_3H_5.NH.CN$, and silver sulphide. If excess of standard silver nitrate be employed, the silver sulphide can be filtered off, and the remaining silver nitrate in the filtrate can then be titrated with ammonium thiocyanate. Weigh 2 grammes of the oil and dissolve in sufficient alcohol (90 per cent) to produce 100 mils. Transfer 5 mils of this solution to a 100-mil flask, add 30 mils of N/10 silver nitrate and 5 mils of Solution of Ammonia. Heat on a water-bath at 80° for thirty minutes with frequent shaking, cool to room temperature, dilute to 100 mils with water, and filter. To 50 mils of the filtrate add 4 mils of concentrated nitric acid and a few drops of ferric sulphate solution (as indicator), and titrate with N/10 ammonium thiocyanate:

$$C_3H_5.N:CS + NH_3 = C_3H_5.NH.CS.NH_2,$$

$$C_3H_5.NH.CS.NH_2 + 2NH_3 + 2AgNO_3 = C_3H_5.NH.CN + Ag_2S + 2NH_4NO_3,$$

$$2AgNO_3 \equiv C_3H_5.N:CS,$$

$$2 \times 170 \equiv 99,$$

$$1000 \text{ mils N/1 } AgNO_3 \equiv 49{\cdot}5 \text{ grammes of } C_3H_5.N:CS,$$

$$1 \text{ mil N/10 } AgNO_3 \equiv 0{\cdot}00495 \text{ gramme of } C_3H_5.N:CS.$$

The Pharmacopœia requires that the oil shall contain not less than 92 per cent *w/v* of allyl iso-thiocyanate.

CHAPTER XXVII

THE AMINES AND RELATED COMPOUNDS

THE ALKYL AMINES

THE alkyl amines are derivatives of ammonia in which one or more of the hydrogen atoms of the NH_3 molecule are displaced by alkyl groups. Amines are distinguished as *primary*, *secondary*, or *tertiary*, according as to whether one, two, or three of the hydrogen atoms have been so displaced. For example :

Primary amine—Methylamine, $CH_3.NH_2$.
Secondary amine—Dimethylamine, $(CH_3)_2NH$.
Tertiary amine—Trimethylamine, $(CH_3)_3N$.

Preparation.—(1) Primary amines can be easily prepared by oxidising the amides of carboxylic acids with sodium hypobromite (a solution of bromine in aqueous sodium hydroxide). In this way methylamine, for example, can be made from acetamide :

$$CH_3.CO.NH_2 + O = CH_3.NH_2 + CO_2.$$

(2) When an alkyl halide is heated in a sealed tube with an alcoholic solution of ammonia, a mixture of primary, secondary, and tertiary amines is produced, the proportion of each depending on the duration of heating, and other conditions. For example :

$$NH_3 + C_2H_5Br = C_2H_5.NH_2 + HBr,$$
$$NH_3 + 2C_2H_5Br = (C_2H_5)_2NH + 2HBr,$$
$$NH_3 + 3C_2H_5Br = (C_2H_5)_3N + 3HBr.$$

At the same time some of the tertiary amine combines with the excess of alkyl halide to form a compound called a " quaternary ammonium salt ", in which the nitrogen atom is quinquevalent :

$$(C_2H_5)_3N + C_2H_5Br = \underset{\text{Tetra-ethyl ammonium bromide.}}{(C_2H_5)_4NBr}.$$

This is the most important general method for the preparation of amines. It suffers from the disadvantage that the mixture of primary, secondary, and tertiary amines obtained can only be separated with great difficulty.

Properties.—The alkyl amines are generally gases or volatile liquids, having a peculiar, fishy, ammoniacal odour. They differ from ammonia in being readily inflammable.

In chemical properties they resemble ammonia in being powerful monacid bases; they turn red litmus blue, and neutralise acids with formation of crystalline salts:

$$CH_3.NH_2 + HCl = \underset{\text{Methylamine hydrochloride.}}{CH_3.NH_2,HCl},$$

$$2(CH_3)_3N + H_2SO_4 = \underset{\text{Trimethylamine sulphate.}}{[(CH_3)_3N]_2,H_2SO_4}.$$

The introduction of alkyl groups into the ammonia molecule actually results in an increase in basic properties. Thus the bases of the series

$$NH_3, \quad CH_3.NH_2, \quad (CH_3)_2NH, \quad (CH_3)_3N,$$

show a progressive increase in strength from left to right.

Primary, secondary, and tertiary alkyl amines differ in their behaviour towards nitrous acid. This reagent converts primary amines into alcohols. For example:

$$C_2H_5.NH_2 + HNO_2 = C_2H_5.OH + N_2 + H_2O.$$

Secondary amines react with nitrous acid to form compounds called *nitrosamines*:

$$(C_2H_5)_2NH + HNO_2 = \underset{\text{Ethyl nitrosamine.}}{(C_2H_5)_2N.NO} + H_2O.$$

Tertiary amines are not acted upon by nitrous acid.

AMINO-ACIDS

The simpler amino-acids are derived from the fatty acids by displacement of a hydrogen atom of the alkyl radicle by the amino-group, —NH_2.

Carbamic acid, amino-formic acid, $NH_2.COOH$, does not exist in the free state, but many of its derivatives are known. *Ammonium carbamate*, $NH_2.COONH_4$, is one of the constituents of Ammonii Carbonas (see p. 91).

Ethyl carbamate or *urethane*, $NH_2.COOC_2H_5$, can be prepared by the action of ammonia on ethyl chloro-formate:

$$\underset{\text{Ethyl chloro-formate.}}{Cl.COOC_2H_5} + 2NH_3 = NH_2.COOC_2H_5 + NH_4Cl.$$

Urethane is a crystalline solid, melting at 50°.

Glycine, amino-acetic acid, $NH_2.CH_2.COOH$, is the simplest of the amino-acids, and is sometimes obtained by extracting gelatin or glue with dilute sulphuric acid. It can be prepared synthetically, in the form of its ammonium salt, by the action of ammonium hydroxide on mono-chloracetic acid :

$$CH_2Cl.COOH + 3NH_4OH = CH_2(NH_2).COONH_4 + NH_4Cl + 3H_2O.$$

Glycine is a colourless, crystalline solid, melting at 235° ; it is readily soluble in water.

Glycine contains the basic group $-NH_2$, as well as the acidic group $-COOH$. On this account it is neutral to indicators, but is capable of forming salts with both acids and bases. Thus with sodium hydroxide it forms a sodium salt, $NH_2.CH_2.COONa$, and with hydrochloric acid it forms a hydrochloride, $HCl,NH_2.CH_2.COOH$.

Glycine reacts with nitrous acid in the same way as do the primary amines, the $-NH_2$ group being displaced by hydroxyl ; the product is hydroxy-acetic acid, or *glycollic acid*, as it is usually called :

$$NH_2.CH_2.COOH + HNO_2 = \underset{\text{Glycollic acid.}}{HO.CH_2.COOH} + N_2 + H_2O.$$

Many of the more complex amino-acids are important products of animal metabolism, but as they are not of particular interest to the pharmaceutical student, they cannot be dealt with here.

Urea, Carbamide, $CO(NH_2)_2$

Urea can be regarded either as the di-amide of carbonic acid, H_2CO_3, or as the amide of amino-formic acid, $NH_2.COOH$. This will be clear if the formulæ are written as follows :

$$O=C\begin{matrix}\diagup OH\\ \diagdown OH\end{matrix} \qquad O=C\begin{matrix}\diagup NH_2\\ \diagdown OH\end{matrix} \qquad O=C\begin{matrix}\diagup NH_2\\ \diagdown NH_2.\end{matrix}$$

Carbonic acid.   Amino-formic acid.   Urea.

Preparation.—(1) Urea occurs in human urine to the extent of about 3 per cent. It can be isolated from this source by evaporating to small bulk, cooling, and adding concentrated nitric acid. The precipitate of urea nitrate is collected, dissolved in hot water, and treated with barium carbonate to liberate the urea. The solution is then evaporated to dryness, and the urea is separated from the barium nitrate by extracting with alcohol and filtering, when the urea, being soluble in alcohol, can be crystallised from the filtrate.

(2) Urea is usually prepared in the laboratory by evaporating

a solution of ammonium cyanate, when "isomeric change" takes place :

$$\underset{\text{Ammonium cyanate.}}{NH_4.OCN} = CO(NH_2)_2.$$

As a rule, it is more convenient to employ a solution of potassium cyanate and ammonium sulphate in equivalent proportions. The solution is evaporated to dryness on a water-bath, and from the residue the urea is extracted with alcohol. The alcoholic solution is filtered, concentrated, and allowed to cool, when the urea crystallises out.

Properties.—Urea crystallises in colourless needles, melting at 128°. It is readily soluble in water and in alcohol, forming neutral solutions.

Urea can be hydrolysed by heating it with water in sealed tubes under pressure :

$$CO(NH_2)_2 + H_2O = CO_2 + 2NH_3.$$

It is more readily hydrolysed by boiling with dilute alkalies or mineral acids.

A solution of sodium hypobromite oxidises urea in the cold, with formation of nitrogen and carbon dioxide :

$$CO(NH_2)_2 + 3NaOBr = CO_2 + N_2 + 3NaBr + 2H_2O.$$

On this reaction depends the "hypobromite process" for the estimation of urea. The sample is shaken, in a bottle connected to a nitrometer, with a solution of sodium hypobromite containing excess of sodium hydroxide. The carbon dioxide is absorbed by the sodium hydroxide, and the volume of the evolved nitrogen can be measured in the nitrometer.

Urea has basic properties, and combines with one equivalent of acids to form crystalline salts, such as the hydrochloride, $CO(NH_2)_2,HCl$. Most of these salts are readily soluble in water, with the exception of the nitrate, $CO(NH_2)_2,HNO_3$, which is only sparingly soluble.

Ureides

These compounds are condensation products of urea with carboxylic acids. Simple members of this class are :

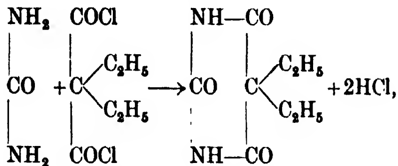
$$\underset{\text{Acetyl urea.}}{NH_2.CO.NH.CO.CH_3} \quad \text{and} \quad \underset{\substack{\text{Biuret} \\ \text{(Amino-formyl urea).}}}{NH_2.CO.NH.CO.NH_2}$$

Dicarboxylic acids condense with urea to form, first, ureido-acids, and then cyclic ureides. Thus, derived from oxalic acid, there are :

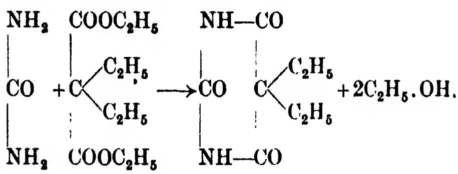
$$\underset{\text{Oxaluric acid.}}{CO\left\langle\begin{matrix}NH_2\\ NH.CO.COOH\end{matrix}\right.} \quad \text{and} \quad \underset{\text{Oxalyl urea.}}{CO\left\langle\begin{matrix}NH.CO\\ |\\ NH.CO\end{matrix}\right.}$$

Ureides can, as a rule, be prepared by the action of the appropriate acid chloride on urea. In chemical properties they resemble the amides (p. 251) in that they have no decided basic or acidic properties. Ureides are usually readily hydrolysed by boiling dilute alkalies, with formation of urea and a salt of the particular acid.

Barbitonum, *Barbitone,* diethyl malonyl urea,[1] sometimes known as *veronal,* is a synthetic ureide of considerable pharmaceutical importance. It is prepared by the interaction of urea with either the acid chloride or the ethyl ester of diethyl malonic acid :



Urea. Diethyl malonyl chloride. Barbitone.



Urea. Ethyl diethyl malonate. Barbitone.

Barbitone is a white crystalline powder, melting at 191°. It is sparingly soluble in water, forming a neutral solution. By fusion with sodium hydroxide it becomes split up, with formation of ammonia, sodium carbonate, and the sodium salt of diethyl acetic acid.

[1] *Malonyl urea,* $CO\left\langle\begin{matrix}NH-CO\\NH-CO\end{matrix}\right\rangle CH_2$, is sometimes called *barbituric acid,* whence the name *diethyl barbituric acid,* by which barbitone is known in Part I. of the Poison Schedule.

CHAPTER XXVIII

THE CARBOHYDRATES

THE class of substances known as the carbohydrates includes the sugars, the starches, and the celluloses, all of which are important vegetable products. These various substances differ widely in physical and chemical properties, but they have in common one peculiarity in composition: they are all built up from the elements carbon, hydrogen, and oxygen, and in every case the ratio of hydrogen atoms to oxygen atoms in the molecule is as 2:1. For example:

Glucose . . .	$C_6H_{12}O_6$.
Cane sugar . . .	$C_{12}H_{22}O_{11}$.
Starch	$C_6H_{10}O_5$.

For this reason all these substances were at one time believed to be "hydrates of carbon", hence the name "carbohydrate". The formula for glucose, for instance, was written $C_6(H_2O)_6$. This view is now known to be incorrect, but it is convenient to retain the old term "carbohydrate" as a general name for the sugars, starches, celluloses, and related compounds.

THE SUGARS

Numerous naturally occurring sugars are known, and they may be conveniently divided into two main groups, namely:

1. The *monosaccharoses*, all of which have the molecular formula $C_6H_{12}O_6$.
2. The *disaccharoses*, all of which have the molecular formula $C_{12}H_{22}O_{11}$.

The various sugars in each group are isomeric, and differ slightly from one another in constitution or configuration.

GLUCOSE, DEXTROSE, GRAPE SUGAR, $C_6H_{12}O_6$

Glucose is present in large quantities in grape juice. It also occurs, mixed with fructose, in many fruits, and in honey.

It can be prepared from the "invert sugar" obtained by the hydrolysis of sucrose with mineral acids (p. 319). Invert sugar, which is a mixture of glucose and fructose, is fractionally crystallised from alcohol. Glucose crystallises out first, leaving the more soluble fructose in solution.

When pure, glucose is a white crystalline powder, but it is more commonly met with as a thick syrup which does not readily crystallise. It is easily soluble in water, and has a sweet taste, though not as sweet as that of sucrose. It chars readily when heated alone or when warmed with concentrated sulphuric acid, evolving vapours having the characteristic odour of "burnt sugar".

The constitutional formula of glucose is

$$CH_2(OH).CH(OH).CH(OH).CH(OH).CH(OH).CHO.$$

The molecule contains four asymmetric carbon atoms, and the full configurational formula is :

$$\begin{array}{rcl} & CH_2.OH & \\ & | & \\ H- & C & -OH \\ & | & \\ H- & C & -OH \\ & | & \\ HO- & C & -H \\ & | & \\ H- & C & -OH \\ & | & \\ & CHO. & \end{array}$$

As can be seen from its formula, glucose is both a polyhydric alcohol and an aldehyde. For this reason it is a powerful reducing agent, and reduces both Fehling's solution and ammoniacal silver nitrate on warming. An aqueous solution of glucose is dextro-rotatory, hence the name "dextrose" by which it is sometimes known.

Glucose, like other aldehydes, reacts with phenylhydrazine to form a phenylhydrazone :

$$\begin{array}{llll} CH_2.OH & & CH_2.OH & \\ | & & | & \\ [CH.OH]_3 & & [CH.OH]_3 & \\ | & & | & \\ CH.OH & & CH.OH & \\ | & & | & \\ CHO & +NH_2.NH.C_6H_5 & CH:N.NH.C_6H_5 & +H_2O. \\ \text{Glucose.} & \text{Phenylhydrazine.} & \text{Glucose phenylhydrazone.} & \end{array}$$

If excess of phenylhydrazine is employed, the glucose phenyl-

ydrazone is oxidised by part of the phenylhydrazine to a ketonic ompound, which immediately reacts with more phenylhydrazine o form a compound called an *osazone*:[1]

$$\begin{array}{lll} CH_2.OH & & CH_2.OH \\ | & & | \\ [CH.OH]_3 & & [CH.OH]_3 \\ | & & | \\ CH.OH \quad + NH_2.NH.C_6H_5 & = & CO \qquad + NH_2.C_6H_5 + NH_3. \\ | & & | \qquad\qquad\quad \text{Aniline.} \\ CH:N.NH.C_6H_5 & & CH:N.NH.C_6H_5 \\ & & \text{Intermediate product.} \end{array}$$

$$\begin{array}{lll} CH_2.OH & & CH_2.OH \\ | & & | \\ [CH.OH]_3 & & [CH.OH]_3 \\ | & & | \\ CO \quad + NH_2.NH.C_6H_5 & = & C:N.NH.C_6H_5 \quad + H_2O. \\ | & & | \\ CH:N.NH.C_6H_5 & & CH:N.NH.C_6H_5 \\ & & \text{Glucose osazone.} \end{array}$$

A solution of glucose is readily fermented by yeast, with formation of alcohol and carbon dioxide.

Tests for Glucose.—(1) When heated alone it chars, giving an odour of burnt sugar.

(2) It chars when warmed with concentrated sulphuric acid, but not so readily as does sucrose.

(3) If glucose is warmed gently with Fehling's solution the latter is reduced, a red precipitate of cuprous oxide being formed (distinction from sucrose).

(4) If a solution of glucose is warmed with ammoniacal silver nitrate a silver mirror is produced (distinction from sucrose).

(5) If glucose is boiled with aqueous sodium hydroxide a brown solution is formed, and on addition of nitric acid an odour of burnt sugar is produced (distinction from sucrose).

(6) In most chemical properties glucose is very similar to lactose. The two sugars can be distinguished from one another by their appearance and physical properties, but a better method of distinction is by boiling a solution of the substance with dilute potassium hydroxide. A solution of glucose darkens in colour, whereas a solution of lactose is almost unaffected.

[1] Glucose osazone (glucosazone) is prepared in the laboratory by adding excess of a mixture of phenylhydrazine and glacial acetic acid to a dilute solution of glucose, and warming on a water-bath. After about ten minutes the osazone separates in small yellow crystals.

GLUCOSUM

Glucose

The official substance is prepared by hydrolysing starch with dilute mineral acids.

It consists mainly of glucose, but the presence of small quantities of other carbohydrates (chiefly dextrin) inhibits its crystallisation. It is an almost colourless, viscous syrup, and gives the reactions previously described for glucose.

Tests for Impurities. *Metallic Compounds* (*Limit of*).—On ignition, it should leave not more than 0·5 per cent of ash.

Moisture (*Limit of*).—2 grammes, dried in a flat-bottomed dish contained in a water-oven, should not lose more than 0·4 gramme.

Sulphite (*Limit of*).—Dissolve 10 grammes in a mixture of 100 mils of water and 10 mils of N/10 iodine; shake well, and titrate immediately with N/10 sodium thiosulphate, using starch mucilage as indicator. Not less than 6·8 mils of the thiosulphate solution should be required.

Arsenic Limit.—2 parts per million (p. 176).

Quantitative Estimation.—There is no official quantitative test, but glucose may be estimated by titration with Fehling's solution, which is a standard solution prepared as follows:

No. 1 Solution :	Copper sulphate	34·64 grammes.
	Concentrated sulphuric acid . .	0·50 mil.
	Distilled water to . . .	500·00 mils.
No. 2 Solution :	Sodium potassium tartrate . .	176·00 grammes.
	Sodium hydroxide . . .	77·00 grammes.
	Distilled water to . . .	500·00 mils.

Mix equal volumes of Solutions 1 and 2 immediately before use. The above quantities are such that 20 mils of Fehling's solution are reduced by 0·10 gramme of glucose with precipitation of the copper as cuprous oxide. Weigh about 2 to 3 grammes of glucose, dissolve, and dilute to 250 mils. Titrate this solution, from a burette, into 20 mils of Fehling's solution contained in a shallow porcelain dish and heated on a water-bath to nearly 100°. The glucose solution should be run in very slowly, with constant stirring. The end-point is shown by the supernatant liquid changing from blue to colourless.

FRUCTOSE, LÆVULOSE, FRUIT SUGAR, $C_6H_{12}O_6$

Fructose occurs, mixed with glucose, in many fruits. It is prepared by separation from "invert sugar" (p. 319), either by fractional crystallisation from alcohol or, better, by taking advantage of the fact that fructose forms an insoluble compound with calcium hydroxide, the corresponding glucose compound being readily soluble. Slaked lime is added, with constant stirring, to a 20 per

cent solution of invert sugar, and the precipitated calcium fructosate, $C_6H_{12}O_6.Ca(OH)_2$, is filtered off, suspended in water, and treated with carbon dioxide, when calcium carbonate is precipitated, leaving fructose in solution.

Fructose forms colourless crystals, readily soluble in water, and in taste it is about as sweet as glucose. It chars when heated alone or with concentrated sulphuric acid.

Fructose has the constitutional formula

$$CH_2(OH).CH(OH).CH(OH).CH(OH).CO.CH_2(OH),$$

and its configurational formula is :

$$\begin{array}{rcl} & CH_2.OH & \\ & | & \\ H— & C & —OH \\ & | & \\ H— & C & —OH \\ & | & \\ HO— & C & —H \\ & | & \\ & CO & \\ & | & \\ & CH_2.OH. & \end{array}$$

It is therefore a polyhydric alcohol and a ketone.[1] Since the simpler ketones are not reducing agents, one might expect that fructose would have no such reducing properties as the aldehydic sugar glucose. The character of the ketonic >CO group is, however, so modified by the presence of the adjacent $—CH_2.OH$ group as to confer upon the molecule powerful reducing properties. Thus fructose, like glucose, rapidly reduces Fehling's solution on warming.

Fructose, on treatment with phenylhydrazine, yields a phenylhydrazone. This, with excess of phenylhydrazine, is converted into an osazone by reactions similar to those described in the case of glucose. It is interesting to note that the osazone formed from fructose is identical with that formed from glucose :

$$\begin{array}{lclclcl} CH_2.OH & & CH_2.OH & & CH_2.OH & & CH_2.OH \\ | & & | & & | & & | \\ [CH.OH]_3 & & [CH.OH]_3 & & [CH.OH]_3 & & [CH.OH]_3 \\ | & \rightarrow & | & \rightarrow & | & \rightarrow & | \\ CO & & C:N.NH.C_6H_5 & & C:N.NH.C_6H_5 & & C:N.NH.C_6H_5 \\ | & & | & & | & & | \\ CH_2.OH & & CH_2.OH & & CHO & & CH:N.NH.C_6H_5. \\ \text{Fructose.} & & \text{Fructose phenyl-hydrazone.} & & \text{Intermediate product.} & & \text{Glucose osazone.} \end{array}$$

[1] Monosaccharoses which, like glucose, contain an aldehyde group are sometimes called aldoses; those which, like fructose, contain a ketone group are sometimes called ketoses.

Fructose is lævo-rotatory, and rotates the plane of polarisation to the left to a greater extent than glucose does to the right. It ferments readily with yeast in aqueous solution, yielding alcohol and carbon dioxide.

SUCROSE, CANE SUGAR, $C_{12}H_{22}O_{11}$

Sucrose occurs in large quantities in the sugar-cane and in the sugar-beet. The juice of the sugar-cane is expressed by crushing between rollers ; in the case of the sugar-beet the sugar is extracted by soaking the beet, in the form of thin slices, in water. In either case the solution of crude sucrose obtained is boiled with a little milk of lime to precipitate albuminous matter, treated with carbon dioxide to precipitate the lime as calcium carbonate, and filtered. The clear filtrate is evaporated and allowed to cool, when the sugar is deposited in brown crystals, leaving a dark mother-liquor known as "molasses". If pure white sugar is required, the solution of brown sugar is decolorised by filtration through animal charcoal, and is then evaporated to crystallisation under diminished pressure in vacuum pans.

Sucrose crystallises in colourless prisms. It is more soluble in water, and is sweeter, than glucose. When heated it melts, gradually darkens in colour, forming "burnt sugar" or caramel, and finally chars, evolving vapours with an odour of burnt sugar. It chars very readily with concentrated sulphuric acid on gentle warming.

Sucrose is dextro-rotatory in aqueous solution. It has no reducing properties, and is without action on Fehling's solution and on ammoniacal silver nitrate.

If sucrose is boiled with dilute sulphuric acid it undergoes hydrolysis, a mixture of equal proportions of glucose and fructose being produced :

$$C_{12}H_{22}O_{11} + H_2O = \underset{\text{Glucose.}}{C_6H_{12}O_6} + \underset{\text{Fructose.}}{C_6H_{12}O_6}$$

Since fructose rotates the plane of polarisation of polarised light to the left to a greater extent than glucose does to the right, the mixture of sugars produced is slightly lævo-rotatory. The original sucrose was dextro-rotatory. Hence, during the process of hydrolysis, the optical rotation of the solution has undergone an inversion or change from dextro- to lævo-. The mixture of sugars produced is therefore called *invert sugar.*

This hydrolysis or inversion of sucrose can also be brought about by an enzyme, invertase, which is present in yeast. In this case the mixture of glucose and fructose produced is fermented by the action of the zymase in the yeast, forming alcohol and carbon dioxide. Sucrose can therefore be fermented by yeast, though not so rapidly as can glucose and fructose.

Tests for Sucrose.—(1) When heated it melts and then chars, giving an odour of burnt sugar.

(2) It chars very readily when gently warmed with concentrated sulphuric acid.

(3) It does not reduce Fehling's solution or ammoniacal silver nitrate (distinction from glucose).

(4) If a little sucrose be inverted by boiling for five to ten minutes with dilute sulphuric acid, cooled, made slightly alkaline with sodium hydroxide, and warmed with Fehling's solution, the solution is reduced, cuprous oxide being precipitated.

SACCHARUM PURIFICATUM

Refined Sugar. *Syn.* Sucrose

This is the purified sugar obtained from the juice of the sugar-cane, sugar-beet, sugar-maple, or Chinese sugar-maple.

It forms colourless crystals or crystalline masses, soluble 1-0·45 in water, and 1-100 in alcohol.

Tests for Impurities. *Metallic Compounds (Limit of).*—On ignition, it should yield not more than 0·05 per cent of ash.

Barium and Strontium.—The aqueous solution should yield no turbidity on addition of dilute sulphuric acid.

Calcium.—The aqueous solution should give no precipitate on the addition of ammonium hydroxide and ammonium oxalate.

Sulphate.—The aqueous solution, acidified with hydrochloric acid, should yield no turbidity on addition of barium chloride.

Chloride.—The aqueous solution, acidified with dilute nitric acid, should not become opalescent on the addition of silver nitrate.

Glucose.—A concentrated solution, heated on a water-bath to about 82° with Fehling's solution, should not yield more than a trace of red or yellow precipitate. The B.P.C. states that a solution of sucrose should not yield more than a slight coloration when boiled with ammoniacal silver nitrate.

Ultramarine and other Colouring Matter.[1]—It should be completely soluble in half its weight of water, forming a clear, colourless, and odourless syrup, which, when acidified with hypophosphorous acid and allowed to stand for twenty-four hours, should not develop an unpleasant odour.

LACTOSE, MILK SUGAR, $C_{12}H_{22}O_{11}$

This sugar occurs to the extent of about 5 per cent in milk, from which it can be obtained by adding rennet to precipitate the protein,

[1] The yellow tinge of impure sugar is sometimes masked by the addition of blue colouring matter such as Prussian blue or ultramarine. The latter is an artificial pigment made by strongly heating a mixture of sodium carbonate, kaolin, charcoal, and sulphur.

casein (curds), filtering, and evaporating the clear filtrate (whey) to small bulk. Lactose crystallises out on cooling.

Lactose is a comparatively sparingly soluble sugar, and is not very sweet. It reduces Fehling's solution, but does not ferment readily with yeast. It forms an osazone with phenylhydrazine.

When lactose is boiled with dilute sulphuric acid it yields a mixture of glucose and a sugar called *galactose*:

$$\underset{\text{Lactose.}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Glucose.}}{C_6H_{12}O_6} + \underset{\text{Galactose.}}{C_6H_{12}O_6}.$$

Tests for Lactose.—(1) When heated alone it goes brown, and finally chars, giving an odour of burnt sugar.

(2) It chars when gently warmed with concentrated sulphuric acid.

(3) It reduces Fehling's solution on warming (distinction from sucrose).

(4) When lactose is boiled with aqueous sodium hydroxide a brown solution is formed, which, on addition of nitric acid, gives an odour of burnt sugar (distinction from sucrose).

(5) Lactose can be distinguished from glucose by its appearance and physical properties, and by the fact that it does not darken appreciably when warmed with dilute potassium hydroxide.

SACCHARUM LACTIS

Milk Sugar. *Syn.* Lactose

The official substance occurs in crystalline masses or as a white powder, containing one molecule of water of crystallisation. Soluble 1·7 in cold water and about 1·1 in boiling water. Unlike sucrose, it is practically insoluble in alcohol (90 per cent).

Tests for Impurities. *Metallic Compounds* (*Limit of*).—On ignition, it should leave not more than 0·25 per cent of ash.

Lactic and other Acids (*Limit of*).—5 grammes dissolved in water should require not more than 1·5 mils of N/10 sodium hydroxide for neutralisation, using phenolphthalein as indicator.

Sucrose.—Shake 5 grammes well with 20 mils of alcohol (90 per cent), and filter. The filtrate should leave no appreciable residue when evaporated on a water-bath.

MALTOSE, MALT SUGAR, $C_{12}H_{22}O_{11}$

Maltose is a sugar formed by the action of the enzyme diastase, contained in malt, on starch. It is an intermediate product in the manufacture of alcohol (p. 219).

Maltose is a crystalline solid, very readily soluble in water. It reduces Fehling's solution, ferments readily with yeast, and is dextro-rotatory.

On boiling with dilute sulphuric acid, maltose is converted into glucose:

$$\underset{\text{Maltose.}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Glucose.}}{2C_6H_{12}O_6}.$$

STARCHES AND CELLULOSES

Starch is one of the main constituents of many plants, notably potatoes and cereals. Much of the starch of commerce is potato starch, which can be prepared in a simple manner by macerating the potatoes with water and straining through fine sieves. The turbid liquid which passes through the sieves slowly deposits the starch as a white paste.

Starch is a white, amorphous substance, composed of microscopic granules. Starches obtained from different plants do not differ much in appearance or in chemical composition, but they can be readily distinguished from one another by the appearance of the granules as seen under the microscope.

Starch granules consist mainly of true starch, or granulose, surrounded by a thin layer of starch cellulose. The granules are insoluble in cold water. When boiled with water they swell and burst, with formation of a translucent liquid, which, if sufficiently concentrated, sets on cooling to a jelly (starch mucilage). The liquid, which contains the granulose in solution or colloidal suspension, can be separated from the cellulose by filtration, and, from the filtrate, addition of alcohol precipitates the granulose in the form of a white amorphous powder—the so-called "soluble starch".

When starch is heated to about 200° it is converted into *dextrin*, a white powder which, on treatment with water, forms a sticky mucilage which is used as a substitute for gum.

When boiled with dilute sulphuric acid, starch is converted first into dextrin and finally into glucose. The enzyme diastase, present in malt, is capable of converting starch into maltose.

The formula of starch is written $(C_6H_{10}O_5)_n$, since, although its empirical formula, calculated from the results of analyses, appears to be $C_6H_{10}O_5$, nothing is known of its molecular formula, except that it is some very high multiple of the empirical formula.

Amylum. *Starch.*—This is obtained from wheat, maize, or rice. The crushed grain contains, in addition to starch, a sticky, nitrogenous substance known as gluten. The gluten can be removed, either by extraction with very dilute sodium hydroxide, in which it is soluble, or by macerating the grain with water and allowing to stand, when the gluten undergoes a process of fermentation, being thus converted into soluble substances which can be removed by washing. In either case the liquid containing the starch in suspension is passed through sieves to remove extraneous matter, the starch being finally collected on linen cloth or very fine calico and dried.

Starch is met with as a white powder, or in irregular angular or columnar masses. The various official varieties can be easily distinguished by their appearances under the microscope, which are as follows.—1. Wheat Starch: A mixture of large and small granules, the former lenticular in shape, and marked with faint concentric striæ surrounding a nearly central hilum. 2. Maize Starch: Granules more uniform in size, frequently polygonal, somewhat smaller than the large granules of wheat starch, and having a very distinct hilum, but without evident concentric striæ. 3. Rice Starch: Granules extremely minute, nearly uniform in size, polygonal, without evident hilum or striæ. Starch should be free from granules other than those described. The presence of potato starch, the most likely adulterant, can be easily recognised, since its granules are very much larger than those of any of the official varieties.

Tests for Starch.—(1) Starch can be recognised by its appearance, and by the peculiar gelatinous mass produced on boiling with water and cooling.

(2) Starch chars when heated alone, giving an unpleasant odour. It also chars when gently warmed with concentrated sulphuric acid.

(3) The following is a very characteristic and delicate reaction: A very small quantity of starch is boiled with water, and the liquid is cooled and treated with a few drops of iodine solution. An intense blue colour is produced, which disappears on boiling.

CELLULOSE, $(C_6H_{10}O_5)_x$

Cellulose is the chief component of the cell walls of all vegetable tissues. Cotton, linen, and filter-paper are all fairly pure forms of cellulose.

Cellulose is insoluble in water and in ordinary organic solvents, but is slowly dissolved by concentrated sulphuric acid. The solution, when diluted with water and boiled, yields glucose. Cellulose is also soluble in an ammoniacal solution of cupric hydroxide, and on this fact depends one of the earlier methods for the manufacture of artificial silk.

The molecular formula of cellulose, like that of starch, is unknown.

Gun-cotton is prepared by soaking cotton wool for several hours in a mixture of concentrated sulphuric acid (3 parts) and concentrated nitric acid (1 part). When washed and dried it resembles cotton wool in appearance, but burns with a flash when a light is applied to it. If hit with a hammer or detonated in any way it explodes violently.

The approximate empirical formula of gun-cotton is $C_6H_7O_2(NO_3)_3$.

Pyroxylinum, *Pyroxylin,* is made by soaking cotton wool in a mixture of equal parts of concentrated sulphuric and nitric acids for three minutes only, and then washing free from acid. It is a

less nitrated form of cellulose than gun-cotton, and has the approximate empirical formula $C_6H_8O_3(NO_3)_2$, and it is, therefore, sometimes known as *cellulose dinitrate*.

Pyroxylin is highly inflammable, but it is less explosive than gun-cotton. It also differs from gun-cotton in being soluble in a mixture of alcohol and ether. **Collodium,** *Collodion*, is a solution of pyroxylin (21 grammes) in alcohol (250 mils) and ether (750 mils).

CHAPTER XXIX

BENZENE AND ITS HOMOLOGUES

BENZENE, C_6H_6

BENZENE is a liquid hydrocarbon of great industrial importance.

Preparation.—(1) Benzene is formed, in small quantities, when acetylene gas is heated in a hard glass tube :

$$3C_2H_2 = C_6H_6.$$

By this method it could be built up from its elements, since acetylene can be made from carbon and hydrogen (p. 213).

(2) Benzene is formed when benzoic acid is heated with soda-lime :

$$C_6H_5.COOH + 2NaOH = C_6H_6 + Na_2CO_3 + H_2O.$$

(3) The benzene of commerce is obtained from coal tar. In the process for the manufacture of coal gas, coal is "destructively distilled", or strongly heated out of contact with air. The evolved vapours are passed through a series of condensers, in which a tarry liquid is collected, the gas passing on to be washed in scrubbers, and, after suitable processes of purification, collected in gasometers.[1]

The liquor in the condensers separates into two layers. The upper layer ("ammoniacal liquor") is a dirty, aqueous solution containing a high percentage of ammonium salts (p. 32). The lower layer is a dark brown oily liquid known as coal tar.[2] Coal tar contains a great variety of organic compounds, and is our chief source of benzene, toluene, phenol and the cresols, naphthalene,

[1] The approximate composition of coal gas is as follows :

Hydrogen	50 per cent by volume
Methane	35 ,, ,, ,,
Carbon monoxide	5 ,, ,, ,,
Illuminants	5 ,, ,, ,,

together with smaller proportions of other gases. The illuminants, which cause coal gas to burn with a yellow luminous flame, include ethylene, acetylene, and benzene vapour.

Different samples of coal gas vary considerably in composition.

[2] **Pix Carbonis Præparata,** *Prepared Coal Tar,* is prepared from commercial coal tar by heating at 50° for an hour, in order to drive off the more volatile constituents.

and other important substances. These various components are all separated from the tar by an intricate process of fractional distillation. The lowest boiling-point fraction (below 140°) is agitated, first with concentrated sulphuric acid and then with aqueous caustic soda, and is finally washed with water. The neutral oil thus obtained consists chiefly of benzene, and is further purified by fractional distillation.

Properties.—Benzene is a colourless, very mobile liquid, of specific gravity 0·88. It boils at 80°, and freezes to a crystalline solid when cooled to 6°. It is insoluble in water, but is miscible with alcohol and ether. It is very inflammable, burning with a yellow smoky flame.

In chemical properties benzene differs widely from any of the hydrocarbons already considered. It *resembles* the paraffins in being exceedingly stable. It is unaffected by boiling alkalies, and is only very slowly attacked by such powerful oxidising agents as potassium permanganate. It reacts slowly with chlorine under ordinary conditions, yielding substitution products, such as chlorobenzene, C_6H_5Cl, and dichlorobenzene, $C_6H_4Cl_2$. Benzene *differs* from the paraffins in that it can, under certain conditions, yield additive products. Thus if a mixture of benzene and hydrogen is passed over heated nickel, direct combination takes place, with formation of *hexahydrobenzene*, C_6H_{12}:

$$C_6H_6 + 3H_2 = C_6H_{12}.$$

A most important difference between benzene and the hydrocarbons previously dealt with lies in its behaviour towards concentrated sulphuric and nitric acids. When benzene is boiled with concentrated sulphuric acid it is slowly converted into a substance called benzene sulphonic acid:

$$C_6H_6 + H_2SO_4 = \underset{\text{Benzene sulphonic acid.}}{C_6H_5.SO_3H} + H_2O.$$

If heated with concentrated nitric acid it is converted into nitrobenzene:

$$C_6H_6 + HNO_3 = \underset{\text{Nitrobenzene.}}{C_6H_5.NO_2} + H_2O.$$

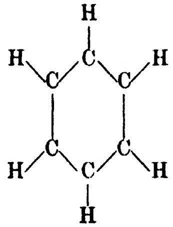
Constitution.—The molecular formula of benzene, as given by analyses and molecular weight determinations, is C_6H_6. The six-carbon member of the paraffin series is C_6H_{14}. Owing to the small number of hydrogen atoms in the molecule, it might appear at first sight that any constitutional formula for benzene must necessarily represent it as being highly unsaturated, and as containing a number of double or treble bonds. But benzene does not behave like an

ordinary unsaturated compound; it is a very stable compound, and only yields derivatives, as a general rule, by a process of substitution, although, under certain circumstances, it can form additive derivatives. We must therefore seek for some constitutional formula which is capable of explaining these facts.

Benzene is the parent substance of a large group of organic compounds, all of which contain six or more carbon atoms in the molecule. These compounds can be made to undergo various chemical changes in the course of which one or more carbon atoms are sometimes eliminated from the molecule. It has, however, been found impossible to reduce the number of carbon atoms to less than six without causing complete disintegration of the molecule. Benzene itself can be converted into numerous substitution products by displacement of the hydrogen atoms by various atoms or groups; but, here again, it is impossible to remove a carbon atom from benzene without considerable difficulty and without breaking up the molecule. It is, therefore, evident that the molecules of benzene and its derivatives contain an exceedingly stable nucleus of six carbon atoms.

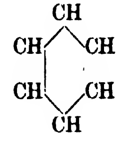
The mono-substitution derivatives of benzene exist in only one form. There is, for example, only one bromobenzene, C_6H_5Br, although three isomeric dibromobenzenes, $C_6H_4Br_2$, are known. Further, it has been found possible, by indirect methods, to prepare a number of samples of mono-bromobenzene by displacement of different hydrogen atoms of the molecule by bromine atoms, and all these samples have been proved to be identical in every respect. The hydrogen atoms in benzene must, therefore, be symmetrically arranged within the molecule.

These two important conclusions—that the benzene molecule contains a stable nucleus of six carbon atoms, and that the hydrogen atoms are symmetrically arranged with respect to the rest of the molecule—have led to the view that the molecule of benzene consists of a symmetrical closed chain or ring of six carbon atoms, and that one hydrogen atom is attached to each carbon atom, thus:



I.

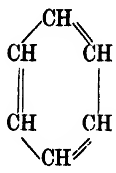
or



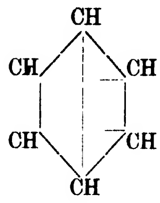
II.

It will be noticed that, in this formula, the fourth valency bond of each carbon atom is omitted. The dispositions of these fourth

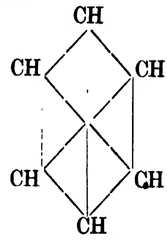
valency bonds have given rise to much controversy, and numerous formulæ for benzene have been suggested, such as :



Kekule's formula.

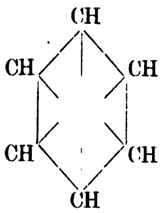


Ladenburg's formula.



Claus' formula.

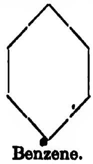
A commonly accepted view is that the fourth valency bonds are simply directed towards the centre of the nucleus, without actually linking opposite pairs of carbon atoms together :



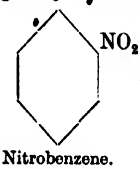
Baeyer's centric formula.

This last formula expresses well the exact symmetry of the molecule, and, whilst not representing benzene as an ordinary unsaturated compound, it accounts for the fact that benzene can, under certain conditions, add on directly as many as six univalent atoms or groups. For ordinary purposes the exact disposition of the fourth valency bonds is a question of little importance, and it is usual to employ the simple Formula I. or II.

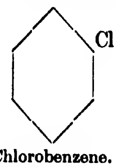
For purposes of abbreviation benzene is sometimes represented by a plain hexagon, the symbols for carbon and hydrogen being omitted. This makes it possible to write constitutional formulæ of benzene derivatives in a greatly condensed form. For example :



Benzene.



Nitrobenzene.



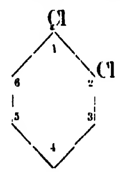
Chlorobenzene.

Benzene and its derivatives are known collectively as the *aromatic compounds*, as distinguished from the open-chain or *aliphatic*

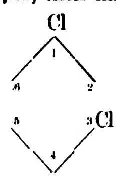
compounds. The term "aromatic" originated from the fact that the first benzene derivatives to be studied chemically were mostly pleasant-smelling plant products; the term "aliphatic", or fatty, refers, of course, to the fact that fats and fatty acids are among the most typical of open-chain compounds.

Isomeric Forms of Benzene Derivatives.—It has been pointed out that the mono-substitution derivatives of benzene, such as nitrobenzene, $C_6H_5.NO_2$, can exist in only one form, since it is immaterial which hydrogen atom is displaced by the substituent atom or group.

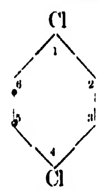
The di-substitution derivatives can exist in three isomeric forms, according as to whether the carbon atoms to which the substituent groups are attached are adjacent, separated by one carbon atom, or separated by two carbon atoms. These three isomeric forms are distinguished by the prefixes ortho-, meta-, and para-, usually contracted to o-, m-, and p-. To take a specific example, there are three isomeric dichlorobenzenes, their names and formulæ being:



o-Dichloro-benzene.



m-Dichloro-benzene.

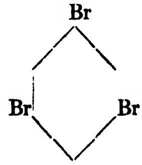


p-Dichloro-benzene.

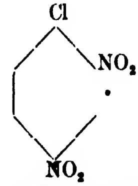
An inspection of these formulæ will show that any di-substitution derivative of benzene can only exist in these three isomeric forms. Instead of the terms ortho, meta, and para, the relative positions of the substituent groups are sometimes indicated by numbers. Thus the three dichlorobenzenes may be named as follows:

1, 2-Dichlorobenzene (ortho).
1, 3-Dichlorobenzene (meta).
1, 4-Dichlorobenzene (para).

Tri- and tetra-substitution products of benzene can also exis in isomeric forms, and in these cases the isomers are nearly alway distinguished by numbers; for example:



1, 3, 5-Tribromobenzene.

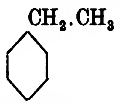


1-Chloro-2, 4-Dinitrobenzene.

Benzenum. *Benzene.*—This is required to have a specific gravity from 0·880 to 0·887, and 95 per cent of it should distil between 79° and 82°. It should solidify when cooled to 0°, and should not entirely remelt below 4°.

Homologues of Benzene

The homologues of benzene contain one or more alkyl groups in place of hydrogen atoms. A typical example is ethyl benzene, $C_6H_5.CH_2.CH_3$:



Ethyl benzene.

A molecule like this can be seen to consist of two parts, which may be described as the nucleus or ring, and the side chain. Even when the alkyl group contains only one carbon atom, as in toluene, $C_6H_5.CH_3$, it is often referred to as the "side chain".

Toluene, methylbenzene, $C_6H_5.CH_3$, is the first homologue of benzene. It occurs in considerable quantities in coal tar, and this is the source from which it is usually obtained. It can, however, be prepared from benzene by the following important synthetic methods:

1. *Reaction of Friedel and Crafts.*—Dry benzene is treated with a methyl halide, in the presence of anhydrous aluminium chloride as catalyst:

$$C_6H_6 + CH_3Br = C_6H_5.CH_3 + HBr.$$

2. *Fittig's Reaction.*—A mixture of a mono-halogen derivative of benzene with a methyl halide is treated with sodium:

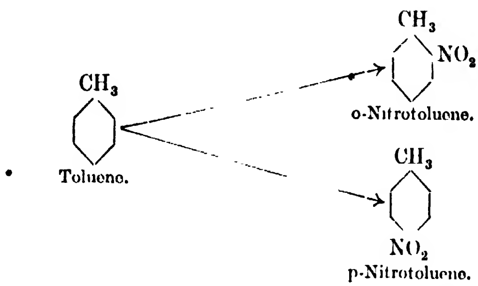
$$C_6H_5I + CH_3I + 2Na = C_6H_5.CH_3 + 2NaI.$$

These two reactions are general methods for the synthesis of aromatic hydrocarbons, and by employing different alkyl halides various homologues of benzene can be prepared. Fittig's reaction, it should be noted, is similar to the Würtz method (p. 206) for the preparation of ethane.

Toluene is a colourless liquid with an odour very similar to that of benzene. Specific gravity, 0·88; boiling-point, 110°. It is inflammable, and burns with a smoky flame.

Toluene closely resembles benzene in many of its chemical properties. It slowly reacts with chlorine or bromine, forming

substitution products (p. 205). When heated with nitric acid it yields a mixture of o- and p-nitrotoluenes :



Similarly, when heated with sulphuric acid, it yields a mixture of o- and p-toluene sulphonic acids, $C_6H_4(CH_3).SO_3H$.

Toluene differs from benzene in that it is comparatively easily oxidised by prolonged boiling with potassium permanganate solution, the methyl group being converted into —COOH :

$$C_6H_5.CH_3 + 3O = C_6H_5.COOH + H_2O.$$

Benzoic acid.

Most benzene homologues can be oxidised to carboxylic acids in this way, each side-chain, no matter how long, being oxidised to —COOH. Thus ethyl benzene, like toluene, is oxidised to benzoic acid :

$$C_6H_5.CH_2.CH_3 + 6O = C_6H_5.COOH + CO_2 + 2H_2O.$$

Ethylbenzene, $C_6H_5.CH_2.CH_3$, is isomeric with the three **dimethylbenzenes** or **xylenes**, $C_6H_4(CH_3)_2$. All these compounds are volatile liquids, very similar in properties to toluene. Ethyl benzene can be prepared from benzene and ethyl bromide by Friedel and Crafts' reaction :

$$C_6H_6 + C_2H_5Br = C_6H_5.C_2H_5 + HBr.$$

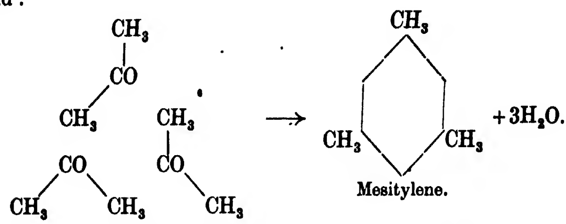
o-Xylene is best prepared from o-bromotoluene and methyl bromide by Fittig's reaction :

$$C_6H_4(CH_3)Br + CH_3Br + 2Na = C_6H_4(CH_3)_2 + 2NaBr.$$

m- and p-xylenes can be made in a similar way, using m- and p-bromotoluenes.

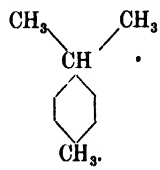
Mesitylene, 1,3,5-trimethylbenzene, $C_6H_3(CH_3)_3$, is a particularly interesting hydrocarbon, as its method of preparation forms a connecting link between the aliphatic and aromatic compounds.

It is made by distilling acetone with fairly concentrated sulphuric acid :



Mesitylene.

Cymene, p-methyl-isopropylbenzene, $C_6H_4(CH_3)C_3H_7$, occurs in Oleum Ajowan and certain other essential oils :



Cymene.

Thymol (p. 351) is a derivative of cymene, and the terpenes (p. 373) are more distantly related to it.

CHAPTER XXX

HALOGEN, SULPHONIC, AND NITRO DERIVATIVES OF THE AROMATIC HYDROCARBONS

The Aryl Radicles.—The univalent groups of atoms derived, theoretically, from benzene and its homologues by the loss of a hydrogen atom are called the aryl radicles. The aryl radicles thus bear the same relationship to the benzene hydrocarbons as the alkyl radicles bear to the paraffins. The more important aryl radicles are as follows:

Phenyl, C_6H_5—	derived from benzene, C_6H_6.
o-Tolyl, $C_6H_4(CH_3)$—	derived from toluene, $C_6H_5.CH_3$, by removal of a hydrogen atom from the nucleus.
m-Tolyl, $C_6H_4(CH_3)$—	
p-Tolyl, $C_6H_4(CH_3)$—	
Benzyl, $C_6H_5.CH_2$—	derived from toluene by removal of a hydrogen atom from the side-chain.

Halogen Compounds

Action of Chlorine on Benzene.—When benzene is subjected to the action of a stream of chlorine gas at ordinary temperatures, and in the absence of strong sunlight, a number of substitution products are formed, just as in the action of chlorine on methane. Among these products are chlorobenzene, C_6H_5Cl, and o- and p-dichlorobenzenes, $C_6H_4Cl_2$. The velocity of the reaction is greatly increased by the presence of a trace of iodine or a little metallic iron or aluminium, all of which act as catalysts or " halogen carriers ".

If, however, benzene is treated with chlorine in bright sunlight, additive products are formed. For example:

$$C_6H_6 + 3Cl_2 = \underset{\text{Benzene hexa-chloride.}}{C_6H_6Cl_6}.$$

Action of Chlorine on Toluene.—When toluene is treated with chlorine at ordinary temperatures, and in the absence of direct

sunlight, it is slowly converted into a mixture of o- and *p*-chlorotoluenes, $C_6H_4\langle{}^{CH_3}_{Cl}$, by displacement of hydrogen atoms of the nucleus. As in the case of benzene, the *reaction proceeds much more rapidly in the presence of a carrier.*

When toluene is treated with chlorine at boiling-point, or in bright sunlight, substitution takes place in the side-chain, with formation of a mixture of the following products, the proportion of each depending upon the duration of chlorination :

Benzyl chloride . . .	$C_6H_5.CH_2Cl$.
Benzal dichloride . . .	$C_6H_5.CHCl_2$.
Benzo-trichloride . . .	$C_6H_5.CCl_3$.

Other homologues of benzene behave in a similar way. If chlorinated in the cold, in absence of bright sunlight, and preferably in presence of a carrier, substitution takes place in the nucleus; but if chlorinated at boiling-point, or in bright sunlight, substitution takes place in the side-chain.

Bromine reacts with benzene and its homologues in a precisely similar way to chlorine. Iodine, on the other hand, is usually without action on aromatic hydrocarbons.

Preparation of Halogen Compounds.—Aromatic compounds *with the halogen in the nucleus* can be most conveniently prepared by one of the following methods :

1. From the solution of a diazonium salt, by Sandmeyer's reaction (p. 344).
2. By the action of a halide of phosphorus on a phenol (p. 347).

Aromatic compounds *with halogen in the side-chain* cannot be prepared from the diazonium salts. They are best made :

1. By direct chlorination of the corresponding hydrocarbon, at boiling-point.
2. By the action of a halide of phosphorus, or an anhydrous halogen acid, on the corresponding aromatic alcohol (p. 356).

Properties.—The aromatic halogen compounds, containing the halogen in the *nucleus*, differ entirely from the aliphatic halogen compounds. They are exceedingly stable compounds, the nuclear halogen atoms being very firmly held. They cannot be hydrolysed by boiling with aqueous acids or alkalies, and are unacted upon by boiling alcoholic potash. *Chlorobenzene* (phenyl chloride), C_6H_5Cl, is a heavy, colourless liquid, with an odour resembling that of benzene, and boils at 132°. It is insoluble in water. *Bromobenzene*, C_6H_5Br, and *iodobenzene*, C_6H_5I, have similar properties, and boil at 155° and 188° respectively. The *o*-, *m*-, and *p-chlorotoluenes* are liquids similar to chlorobenzene.

Compounds containing halogen atoms in the *side-chain* are very much less stable, and the halogen atoms can be easily displaced by the usual hydrolysing agents. *Benzyl chloride*, $C_6H_5.CH_2Cl$, for example, is a colourless fuming liquid, boiling at 176°. It is

insoluble in water, and is hydrolysed, slowly by boiling water, rapidly by boiling aqueous alkalies, with formation of benzyl alcohol:

$$C_6H_5.CH_2Cl + H_2O = C_6H_5.CH_2.OH + HCl.$$

Benzyl alcohol.

This behaviour is exactly similar to that of the alkyl halides. It is, in fact, a general rule that an aromatic compound containing any of the groups —Cl, —Br, —I, —OH, —CHO, —COOH, —CN, —NH_2, etc., in a side-chain, has similar chemical properties to the corresponding aliphatic compounds.

Sulphonic Acids

Benzenesulphonic acid, $C_6H_5.SO_3H$, can be prepared by boiling a mixture of equal volumes of benzene and concentrated sulphuric acid, under a reflux condenser, until the benzene layer has disappeared (6-20 hours):

$$C_6H_6 + H_2SO_4 = C_6H_5.SO_3H + H_2O.$$

The liquid is cooled, poured into cold water, and the solution neutralised with calcium carbonate. In this way the excess of sulphuric acid is precipitated as calcium sulphate, and the benzenesulphonic acid remains in solution as its soluble calcium salt. The solution is filtered, and the filtrate is treated with dilute sulphuric acid, drop by drop, until no further precipitate is formed:

$$(C_6H_5.SO_3)_2Ca + H_2SO_4 = 2C_6H_5.SO_3H + CaSO_4.$$

Calcium benzene-sulphonate.

The solution is again filtered, and the filtrate, which is an aqueous solution of benzenesulphonic acid, is evaporated to a syrup, which crystallises on cooling.

Benzenesulphonic acid forms colourless, deliquescent crystals, very readily soluble in water. The aqueous solution is strongly acid, and dissolves metallic oxides, hydroxides, and carbonates with formation of salts. *Potassium benzenesulphonate*, $C_6H_5.SO_3K$, prepared by neutralising the free acid with potassium carbonate, crystallises in colourless plates with half a molecular proportion of water.

Benzenesulphonic acid, on treatment with phosphorus pentachloride, is converted into *benzenesulphonic chloride*:

$$C_6H_5.SO_3H + PCl_5 = C_6H_5.SO_2Cl + POCl_3 + HCl,$$

Benzene-sulphonic chloride.

and this, on treatment with ammonia, yields *benzene sulphonamide* :

$$C_6H_5.SO_2Cl + NH_3 = \underset{\text{Benzene sulphonamide.}}{C_6H_5.SO_2.NH_2} + HCl.$$

Other Sulphonic Acids.— *Benzene - m - disulphonic acid*, $C_6H_4(SO_3H)_2$, is prepared by prolonged sulphonation of benzene or of benzenesulphonic acid.

When toluene is sulphonated, a mixture of *o-* and *p-toluenesulphonic acids*, $C_6H_4(CH_3).SO_3H$, is formed.

Nitro Compounds

Nitrobenzene, $C_6H_5.NO_2$, is slowly formed when benzene is heated with concentrated nitric acid. It can be more conveniently prepared as follows: A mixture of concentrated nitric acid (60 mils) and concentrated sulphuric acid (60 mils) is slowly added, with constant shaking, to 55 mils of benzene, contained in a flask :

$$C_6H_6 + HNO_3 = C_6H_5.NO_2 + H_2O.$$

The mixture is gently heated on a water-bath for half an hour, cooled, and poured into water. The nitrobenzene sinks to the bottom as a pale yellow heavy oil, which is separated with the aid of a separating funnel, washed with dilute sodium carbonate solution, dried over calcium chloride, and finally purified by distillation.

Nitrobenzene is a pale yellow oily liquid, of specific gravity 1·2 and boiling-point 205°, with a characteristic odour resembling that of almonds. It is insoluble in water, and is volatile in steam. It is largely employed for the preparation of aniline (p. 338).

Other Nitro Compounds.—When nitrobenzene is strongly heated with a mixture of concentrated sulphuric and fuming nitric acids, the nitration proceeds further, and *m-dinitrobenzene*, $C_6H_4(NO_2)_2$, is formed. m-Dinitrobenzene is a pale yellow, crystalline solid, and if nitrated still further it is converted into *symmetrical* or 1, 3, 5-*trinitrobenzene*, $C_6H_3(NO_2)_3$.

When toluene is nitrated as described for the preparation of nitrobenzene, a mixture of *o-* and *p-nitrotoluenes*, $C_6H_4(CH_3).NO_2$, is formed.

The Rule of Substitution.—The student will probably have noticed that, when a second atom or group is introduced into the molecule of a mono-substitution derivative of benzene, the product generally consists either of the meta di-substitution derivative, or of a mixture of the ortho and para. A study of a large number of cases of substitution in the benzene series has led to the formulation of a simple general rule of substitution, which may be stated as follows :

"When a second atom or group is introduced into a benzene nucleus which already contains one substituent, then :

"(*a*) If the original substituent was SO_3H, NO_2, CHO, COOH, $CO.CH_3$, or CN, the main product will be the meta di-substitution derivative.

"(*b*) If, on the other hand, the original substituent was Cl, Br, I, OH, NH_2, or an alkyl group, the product will consist of a mixture of the ortho and para di-substitution derivatives."

This rule is purely empirical, and does not hold in every case. It is, however, sufficiently general to form a useful guide to the position taken up by entering groups, and should be committed to memory.

CHAPTER XXXI

THE AROMATIC AMINES AND DIAZONIUM COMPOUNDS

THE simple aromatic amines resemble the alkyl amines in structure, in that they are derived from ammonia, NH_3, by the substitution of one or more aryl radicles for hydrogen atoms.

In chemical properties the aliphatic and aromatic amines differ widely from one another. The alkyl radicles are somewhat base-forming in character, whereas the aryl radicles are distinctly acid-forming; so that, whilst the introduction of alkyl groups into the NH_3 molecule results in an increase in basic properties, the introduction of aryl groups has the opposite effect. The simplest aromatic amine is phenylamine, or aniline, $C_6H_5.NH_2$. This compound is a much weaker base than ammonia; it does not turn red litmus blue, and its salts are partially hydrolysed in aqueous solution. Diphenylamine, $(C_6H_5)_2NH$, a secondary amine containing two aryl groups, has very feeble basic properties, and only forms salts with concentrated mineral acids. Amines containing three aryl groups, such as triphenylamine, $(C_6H_5)_3N$, have no basic properties at all.

The primary aryl amines also differ from the corresponding alkyl compounds in that, when treated with nitrous acid in the cold, they yield unstable and highly reactive compounds known as diazonium salts (p. 343).

In addition to the purely aromatic amines, such as the examples given above, mixed amines, containing both alkyl and aryl groups, are known. A well-known compound of this type is methylaniline, $C_6H_5.NH.CH_3$. Such compounds are stronger bases than aniline, since the presence of the alkyl groups diminishes, to some extent, the effect of the acidic aryl groups.

ANILINE, PHENYLAMINE, $C_6H_5.NH_2$

Preparation.—Aniline is prepared by reducing nitrobenzene with tin and hydrochloric acid:

$$C_6H_5.NO_2 + 6H = C_6H_5.NH_2 + 2H_2O.$$

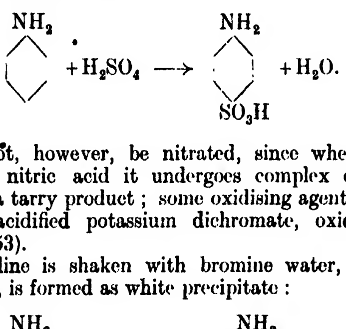
Concentrated hydrochloric acid (100 mils) is added, drop by drop, to a mixture of nitrobenzene (20 mils) and granulated tin

(45 grammes) contained in a flask. The flask is then heated on a water-bath until the odour of nitrobenzene is no longer perceptible. The aniline is present in the form of a complex stannichloride, $(C_6H_5.NH_2,HCl)_2,SnCl_4$, from which it is liberated by adding excess of sodium hydroxide and distilling in a current of steam. The aniline in the distillate is extracted with chloroform, and, after drying the extract over anhydrous potassium carbonate, the solvent is distilled off. The crude aniline remaining is finally purified by distillation.

Properties.—Aniline is a colourless, oily liquid, which darkens on exposure to air. Specific gravity, 1·00; boiling-point, 184°. It has a peculiar characteristic odour, and is sparingly soluble in water, the solution being neutral to indicators.

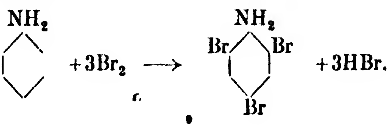
Aniline dissolves readily in dilute mineral acids with formation of salts, such as the hydrochloride, $C_6H_5.NH_2,HCl$, and the sulphate, $(C_6H_5.NH_2)_2,H_2SO_4$. These salts are crystalline solids, and are decomposed in the cold by solutions of alkalies, with liberation of aniline.

Aniline is readily sulphonated by heating it with concentrated sulphuric acid, the main product being aniline p-sulphonic acid or *sulphanilic acid*, $C_6H_4(NH_2).SO_3H$:



Aniline cannot, however, be nitrated, since when treated with concentrated nitric acid it undergoes complex oxidation, with formation of a tarry product; some oxidising agents, such as ferric chloride or acidified potassium dichromate, oxidise aniline to quinone (p. 353).

When aniline is shaken with bromine water, tribromaniline, $C_6H_2Br_3.NH_2$, is formed as white precipitate:



Trichloraniline can be made in a similar way from aniline and chlorine water.

Like all other primary amines, aniline yields an evil-smelling carbylamine when heated with chloroform and alcoholic potash:

$$CHCl_3 + 3KOH + C_6H_5.NH_2 = \underset{\text{Phenyl carbylamine.}}{C_6H_5.NC} + 3KCl + 3H_2O.$$

When aniline is treated with sodium nitrite in acid solution it is converted into a phenyl diazonium salt (p. 343).

Acetanilidum, *Acetanilide*, $C_6H_5.NH.CO.CH_3$, is formed when aniline is treated, in the cold, with acetyl chloride or acetic anhydride. It is prepared by boiling aniline (10 mils) with glacial acetic acid (12 mils), under a reflux condenser, for several hours:

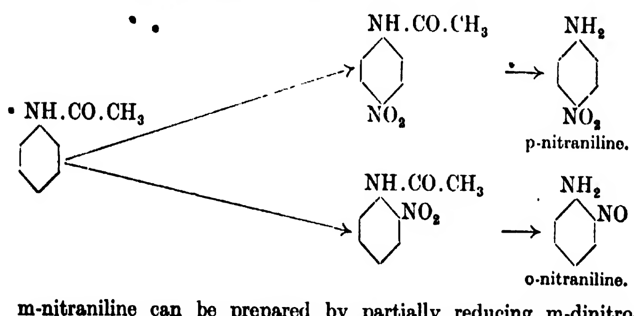
$$C_6H_5.NH_2 + CH_3.COOH = C_6H_5.NH.CO.CH_3 + H_2O.$$

The molten product is poured into cold water, and the crude acetanilide is collected and recrystallised from boiling water or dilute alcohol.

Acetanilide crystallises in colourless, glistening plates, melting at 113°. It is sparingly soluble in water, easily in alcohol, forming neutral solutions. Boiling dilute acids or alkalies slowly hydrolyse it to aniline and acetic acid or their salts:

$$C_6H_5.NH.CO.CH_3 + KOH = C_6H_5.NH_2 + CH_3.COOK.$$

Acetanilide, unlike aniline, can be easily nitrated by heating it with concentrated nitric acid, since the amino group is "blocked", or protected from oxidation, by the introduction of the acetyl group. The product of nitration of acetanilide is a mixture of o- and p-nitro-acetanilides. These nitro-acetanilides, on hydrolysis, yield the corresponding nitranilines:



m-nitraniline can be prepared by partially reducing m-dinitrobenzene with ammonium sulphide:

$$C_6H_4(NO_2)_2 + 6H = C_6H_4(NO_2).NH_2 + 2H_2O.$$

An aqueous solution of acetanilide, containing as little as 1 part in 2000, gives a yellowish-white precipitate on addition of bromine water. This test serves to distinguish acetanilide from phenacetin, since the latter gives no such precipitate.

Tests for Impurities.—Acetanilide should form colourless solutions in concentrated sulphuric acid (absence of readily carbon-

isable organic impurities) and in concentrated nitric acid (absence of phenacetin and phenazone). A cold, saturated aqueous solution should be neutral to litmus (absence of aniline salts and of free acetic acid), and should give no red or green coloration on adding a few drops of ferric chloride solution and allowing to stand (absence of phenazone and salts of aniline).

On ignition, acetanilide should leave not more than 0·1 per cent of ash.

Other Aromatic Amines

The first homologues of aniline are the three **toluidines**—ortho, meta, and para — all of which have the molecular formula $C_6H_4(CH_3).NH_2$. They can be prepared by reducing the corresponding nitro-toluenes with tin and hydrochloric acid in the manner described for the preparation of aniline. They are basic compounds very similar to aniline in chemical properties. The o- and m-compounds are oily liquids, but p-toluidine is a crystalline solid, melting at 45°.

Diphenylamine, $(C_6H_5)_2NH$, is made by strongly heating a mixture of aniline and aniline hydrochloride :

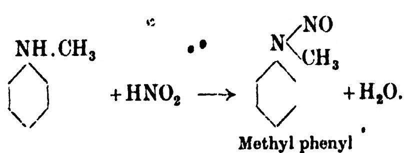
$$C_6H_5.NH_2 + C_6H_5.NH_2,HCl = (C_6H_5)_2NH + NH_4Cl.$$

It is a solid, melting at 54°, and is such a feeble base that its salts are decomposed by cold water. *Triphenylamine,* $(C_6H_5)_3N$, melts at 127° ; it is insoluble in acids.

Methylaniline, $C_6H_5.NH.CH_3$, can be prepared by heating aniline with one equivalent of a methyl halide :

$$C_6H_5.NH_2 + CH_3Br = \underset{\text{Methylaniline hydrobromide.}}{C_6H_5.NH.CH_3,HBr.}$$

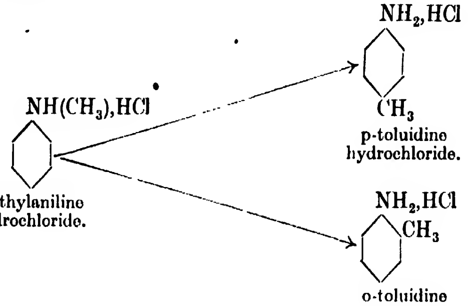
It is a colourless oil, boiling at 192°, and is a stronger base than aniline. Like the secondary alkyl amines, it yields a nitrosamine on treatment with nitrous acid :



Methyl phenyl nitrosamine.

An interesting change takes place when a salt of methylaniline is heated under pressure. The methyl group changes places with a

hydrogen atom of the nucleus, forming a mixture of o- and p-toluidine salts :



Methylaniline hydrochloride.

p-toluidine hydrochloride.

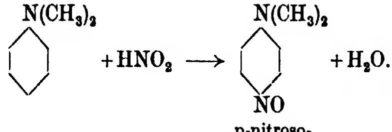
o-toluidine hydrochloride.

Such examples of the migration of atoms or groups from the side-chain to the nucleus are commonly met with among aromatic compounds.

Dimethylaniline, $C_6H_5.N(CH_3)_2$, can be prepared in a manner similar to that described for methylaniline, using excess of the alkyl halide :

$$C_6H_5.NH_2 + 2CH_3Br = \underset{\text{Dimethylaniline hydrobromide.}}{C_6H_5.N(CH_3)_2,HBr} + HBr.$$

It is an oil, boiling at 192°, and has an unpleasant pungent odour. It is a strong base, and forms stable crystalline salts. It differs from the tertiary alkyl amines in that it reacts with nitrous acid, with formation of a nitroso-compound :



p-nitroso-dimethylaniline.

It should be noted that this nitroso-compound is quite different in constitution from the nitrosamines, since the —NO group is attached to a carbon and not to a nitrogen atom.

Benzylamine, $C_6H_5.CH_2.NH_2$, is isomeric with the toluidines and with methylaniline. It can be prepared by heating benzyl chloride with an alcoholic solution of ammonia, a method analogous to that described (p. 309) for the preparation of the alkyl amines :

$$C_6H_5.CH_2Cl + NH_3 = C_6H_5.CH_2.NH_2,HCl.$$

Benzylamine is an example of an aromatic amine containing the

—NH_2 group in the side-chain, and in properties it *closely resembles* the primary alkyl amines. It is a volatile, mobile liquid, boiling at 187°, and is readily soluble in water, forming a *strongly alkaline* solution. When treated with nitrous acid it does not yield a diazonium salt, but is converted into benzyl alcohol:

$$C_6H_5.CH_2.NH_2 + HNO_2 = C_6H_5.CH_2.OH + N_2 + H_2O.$$

The Diazonium Compounds

If a cold solution of aniline in dilute hydrochloric acid is treated with sodium nitrite the liberated nitrous acid converts the aniline into a compound called phenyl diazonium chloride:

$$C_6H_5.NH_2,HCl + HNO_2 = \underset{\text{Phenyl diazonium chloride.}}{C_6H_5.N:NCl} + 2H_2O.$$

This compound is a salt of a strong base, phenyl diazonium hydroxide, $C_6H_5.N:N.OH$. By treating a solution of aniline in nitric or sulphuric acids with sodium nitrite, phenyl diazonium nitrate, $C_6H_5.N:N.NO_3$, or sulphate, $(C_6H_5.N:N)_2SO_4$, can be obtained.

Other primary aromatic amines which contain the —NH_2 group in the nucleus are converted into diazonium salts by treatment with sodium nitrite in acid solution: p-tolyl diazonium chloride, $C_6H_4(CH_3).N:NCl$, for example, can be prepared by the action of sodium nitrite on a solution of p-toluidine in hydrochloric acid.

The diazonium salts are colourless, crystalline compounds, readily soluble in water. They are, as a rule, very unstable, and many of them are highly explosive in the dry state. The diazonium hydroxides are formed when their salts are treated with silver hydroxide in aqueous solution. For example:

$$C_6H_5.N:NCl + AgOH = C_6H_5.N:N.OH + AgCl.$$

These hydroxides are exceedingly unstable compounds, and, unlike their salts, are of comparatively little importance.

The diazonium salts are very reactive substances, and serve as a starting-point for the preparation of a great number of aromatic compounds. For such synthetic purposes an aqueous solution of a diazonium salt is, as a rule, employed, and it is therefore unnecessary to isolate the salt in the solid state. An aromatic amine can be easily "diazotised", or converted into a solution of a diazonium salt, by dissolving it in excess of a dilute mineral acid (usually hydrochloric acid), cooling the solution in ice or in a freezing mixture, and slowly running in, from a burette, a solution of the theoretical quantity of sodium nitrite. Throughout the process the temperature should not be allowed to rise above about 10°.

Reactions of the Diazonium Salts.—Some of the more important reactions of the diazonium salts will now be briefly described. For convenience, equations will be given representing the reactions of

phenyl diazonium chloride, but it must be understood that, in general, other diazonium salts behave in a precisely analogous manner.

1. On boiling a solution of a diazonium salt, nitrogen is evolved, and a phenol (p. 346) remains in solution :

$$C_6H_5.N:NCl + H_2O = \underset{\text{Phenol.}}{C_6H_5.OH} + N_2 + HCl.$$

2. A dry diazonium salt, on heating with alcohol, yields a hydrocarbon :

$$C_6H_5.N:NCl + C_2H_5.OH = \underset{\text{Benzene.}}{C_6H_6} + CH_3.CHO + N_2 + HCl.$$

3. Aryl chlorides can be made by heating a solution of a diazonium salt with hydrochloric acid in the presence of cuprous chloride, Cu_2Cl_2, as a catalyst (Sandmeyer's reaction) :

$$C_6H_5.N:NCl + HCl = \underset{\substack{\text{Chloro-}\\\text{benzene.}}}{C_6H_5Cl} + N_2 + HCl.$$

Aryl bromides can be made in a similar way, using hydrobromic acid and cuprous bromide, Cu_2Br_2 :[1]

$$C_6H_5.N:NCl + HBr = \underset{\substack{\text{Bromo-}\\\text{benzene.}}}{C_6H_5Br} + N_2 + HCl.$$

Aryl iodides can be made more easily by simply warming the diazonium solution with potassium iodide, no catalyst being required in this case :

$$C_6H_5.N:NCl + KI = \underset{\substack{\text{Iodo-}\\\text{benzene.}}}{C_6H_5I} + N_2 + KCl.$$

4. Aryl cyanides can be prepared by heating a diazonium solution with potassium cyanide in presence of cuprous cyanide (Sandmeyer's reaction) :

$$C_6H_5.N:NCl + KCN = \underset{\substack{\text{Phenyl}\\\text{cyanide.}}}{C_6H_5.CN} + N_2 + KCl.$$

5. By reduction of the diazonium salts, aryl hydrazines[2] are produced. *Phenylhydrazine* is generally prepared by adding stannous chloride and concentrated hydrochloric acid to a diazotised solution of aniline in the cold :

$$C_6H_5.N:NCl + 4H = \underset{\substack{\text{Phenylhydrazine}\\\text{hydrochloride.}}}{C_6H_5.NH.NH_2,\ HCl.}$$

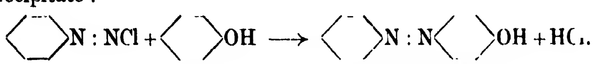
[1] In these reactions, the first product is an additive compound of the diazonium salt with the cuprous halide.

[2] Hydrazine, $NH_2.NH_2$, is an inorganic base.

Phenylhydrazine, when pure, forms colourless crystals, melting at 23°, but it is more frequently met with as a brownish oil, sparingly soluble in water. It is a basic compound, and dissolves readily in dilute mineral acids with formation of salts.

The formation of hydrazones by the action of phenylhydrazine on aldehydes or ketones has already been mentioned (p. 237), as has also the formation of osazones from certain of the sugars (p. 316). On account of these reactions phenylhydrazine is an important reagent.

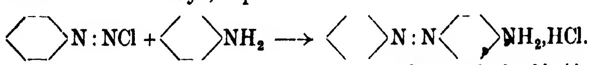
6. When a solution of a diazonium salt is added to an alkaline solution of a phenol (p. 346) or a naphthol (p. 371) a brilliant-coloured compound, of the class known as the "azo-dyes", separates as a precipitate :



Phenol. Hydroxy-azo-benzene.

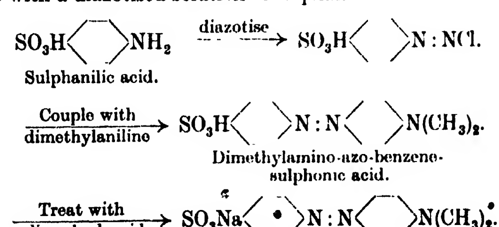
In this process the linking, or "coupling", of the diazonium compound to the phenol molecule always takes place at either the ortho or the para position to the —OH group.

Azo-dyes can also be made by coupling a diazonium salt with an aromatic amine. If phenyldiazonium chloride is treated with aniline and the mixture warmed, amino-azo-benzene hydrochloride, a salt of a basic azo-dye, is produced :



Amino-azo-benzene hydrochloride.

The indicator *methyl orange* is a familiar example of an azo-dye. It is the sodium salt of the compound obtained by coupling dimethylaniline with a diazotised solution of sulphanilic acid :



Methyl orange.

Most of the simpler azo-dyes are bright red, but many brown, yellow, and even blue compounds of this type are known.

CHAPTER XXXII

PHENOLS AND THEIR DERIVATIVES

THE phenols are derived from the aromatic hydrocarbons by the substitution of one or more —OH groups for hydrogen atoms of the nucleus. The phenols are thus somewhat similar in structure to the aliphatic alcohols, but, chemically, the two classes of compounds have little in common; for whilst the alcohols are perfectly neutral substances, the phenols have distinctly acidic properties, this being due to the effect of the acid-forming aryl group.

PHENOL, $C_6H_5.OH$

Preparation.—(1) Phenol itself, which is the first member of the series, can be made by boiling a diazotised solution of aniline with water:

$$C_6H_5.N:NCl + H_2O = C_6H_5.OH + N_2 + HCl.$$

This provides a method by which phenol can be synthesised from benzene:

$$C_6H_6 \longrightarrow C_6H_5.NO_2 \longrightarrow C_6H_5.NH_2 \longrightarrow C_6H_5.N:NCl \longrightarrow C_6H_5.OH.$$

(2) Phenol can be prepared, in the form of its potassium salt, by fusing potassium benzene sulphonate with potassium hydroxide in an iron crucible:

$$C_6H_5.SO_3K + 2KOH = \underset{\text{Potassium phenate.}}{C_6H_5.OK} + K_2SO_3 + H_2O.$$

In order to obtain free phenol the melt is allowed to cool, dissolved in water, and treated with excess of hydrochloric acid. The liberated phenol is extracted with ether, and, after evaporating off the solvent, the product is purified by distillation.

(3) The phenol of commerce is obtained as one of the products of the fractional distillation of coal tar (p. 325).

The fraction collected between 170° and 230° ("middle oil") consists chiefly of phenol and naphthalene (p. 370). It is allowed

to cool, when most of the naphthalene crystallises out, and is separated. The remaining oil is shaken with warm sodium hydroxide solution, which dissolves out the phenol as sodium phenate; the aqueous layer is then run off from the insoluble portion of the oil and treated with dilute sulphuric acid, which liberates the phenol, the product being finally purified by distillation.

Properties.—Phenol forms colourless, deliquescent crystals with a characteristic odour, which turn pink on prolonged exposure to air. Phenol melts at 42°, boils at 183°, and is volatile in steam. It is soluble about 1 in 12 in water, and the pure substance or its solution has a caustic action on the skin.

Though neutral to litmus, phenol has distinct acidic properties. It does not react with metallic carbonates, but dissolves freely in solutions of sodium or potassium hydroxide, with formation of the corresponding *phenate*:

$$C_6H_5.OH + NaOH = \underset{\text{Sodium phenate.}}{C_6H_5.ONa} + H_2O.$$

On evaporating the solution the phenate can be obtained as a colourless, deliquescent, crystalline solid. The phenates, unlike the alcoholates (p. 216), are thus stable towards water; they are, however, immediately decomposed by acids, or even by carbon dioxide, with liberation of phenol.

When phenol is treated with phosphorus pentachloride, chlorobenzene is formed. This reaction is analogous to the formation of ethyl chloride from ethyl alcohol:

$$C_6H_5.OH + PCl_5 = C_6H_5Cl + POCl_3 + HCl.$$

Compare $$C_2H_5.OH + PCl_5 = C_2H_5Cl + POCl_3 + HCl.$$

When bromine water is added to an aqueous solution of phenol a white precipitate of 2, 4, 6-tribromophenol is produced (compare aniline, p. 339).

When phenol is heated with concentrated sulphuric acid a mixture of phenol o- and p-sulphonic acids is formed:

$$C_6H_5.OH + H_2SO_4 = C_6H_4(OH).SO_3H + H_2O.$$

Phenol is very easily nitrated, even by dilute nitric acid, with formation of a mixture of o- and p-nitrophenols, $C_6H_4(OH).NO_2$. These compounds, on further nitration with concentrated nitric acid, are converted into trinitrophenol or picric acid, $C_6H_2(NO_2)_3.OH$.

Towards oxidising agents phenol behaves somewhat like a tertiary alcohol. It can only be oxidised with difficulty, and the process results in the breaking up of the molecule.

An aqueous solution of phenol becomes deep blue on addition of ferric chloride solution—a reaction common to many aromatic compounds containing an —OH group in the nucleus.

When sodium or potassium phenate is heated with a methyl halide, *anisole*, or phenyl methyl ether, $C_6H_5.O.CH_3$, is produced:[1]

$$C_6H_5.OK + CH_3Br = C_6H_5.O.CH_3 + KBr.$$

Phenetole, or phenyl ethyl ether, $C_6H_5.O.C_2H_5$, can be prepared in a similar way from potassium phenate and an ethyl halide.

ACIDUM CARBOLICUM

Phenol

The official substance forms small deliquescent crystals, which should be colourless, but may acquire a pinkish tinge on exposure to moist air. Its odour should not be fetid or tarry. At 15·5° 100 parts of phenol are liquefied by the addition of 10 parts of water, form a clear liquid with 30-40 parts of water, and are completely dissolved by 1200 parts of water, the aqueous solution being clear and colourless. Melting point, 39°-40°; boiling point not higher than 183°. Specific gravity at the melting point, 1·060-1·066.

Tests for Impurities. *Free Acid.*—Phenol should not immediately redden blue litmus paper.

Non-volatile Matter.—When evaporated on a water-bath it should leave not more than 0·1 per cent of residue.

Cresol.—1 volume of phenol liquefied by the addition of 10 per cent of water, forms, with 1 volume of glycerin, a clear liquid, which should not be rendered turbid by the addition of 3 volumes of water.

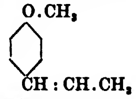
Acidum Carbolicum Liquefactum. *Liquefied Phenol. Syn.* Liquefied Carbolic Acid.—This is prepared by mixing 100 grammes of phenol with sufficient water to produce 115 grammes.

It is a liquid, colourless at first, but usually acquiring a pinkish hue. It forms a clear solution on addition of 12-20 per cent by weight of water at 15·5°. Specific gravity, 1·067-1·069. Boiling point gradually rising to a temperature not higher than 183°.

NITROPHENOLS

A mixture of *o-* and *p-nitrophenols* separates as a dark-coloured, semi-solid mass when phenol is treated in the cold with fairly dilute (30 per cent) nitric acid. The o-compound is separated from the

[1] *Anethole*, which constitutes about 90 per cent of Oleum Anisi, is a derivative of anisole containing an unsaturated side chain.



Anethole.

Anethole is a crystalline solid melting at 21°; it has a strong anise odour.

product by distillation in a current of steam, and the residue, consisting of the p-compound together with resinous matter, is purified by crystallisation from water.

m-Nitrophenol cannot be prepared by nitration of phenol. It is prepared by diazotising m-nitraniline (p. 340) and boiling the solution of the diazonium salt with water :

$$C_6H_4(NO_2).NH_2 \longrightarrow C_6H_4(NO_2).N:NCl \longrightarrow C_6H_4(NO_2).OH.$$

o-, m-, and p-nitrophenols are crystalline compounds, sparingly soluble in water, melting at 45°, 96°, and 114° respectively. The o- and m- are yellow, but the p- is colourless. Only the o- is volatile in steam.

The presence of the $—NO_2$ groups in the molecules of the nitrophenols increases the acidic character of the —OH group. The nitrophenols not only dissolve in solutions of sodium and potassium hydroxides, but decompose solutions of the carbonates, with evolution of carbon dioxide.

Phenacetinum, *Phenacetin,* p-aceto-phenetidine,

$$C_6H_4\begin{cases} O.C_2H_5 \\ NH.CO.CH_3, \end{cases}$$

is an important synthetic drug. It is prepared from p-nitrophenol by the following series of reactions :

$$\underset{\text{p-Nitro-phenol.}}{C_6H_4\begin{cases} OH \\ NO_2 \end{cases}} \xrightarrow[\text{aqueous } K_2CO_3\text{, evaporate, and allow to crystallise}]{\text{dissolve in}} \underset{\text{Potassium p-nitro-phenate.}}{C_6H_4\begin{cases} OK \\ NO_2, \end{cases}}$$

$$\xrightarrow[\text{heat with } C_2H_5Br]{} \underset{\text{p-Nitrophenyl ethyl ether.}}{C_6H_4\begin{cases} O.C_2H_5 \\ NO_2, \end{cases}}$$

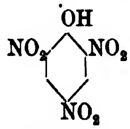
$$\xrightarrow[\text{reduce with nascent hydrogen}]{} \underset{\text{p-Phenetidine.}}{C_6H_4\begin{cases} O.C_2H_5 \\ NH_2, \end{cases}}$$

$$\xrightarrow[\text{heat with glacial acetic acid}]{} \underset{\text{Phenacetin.}}{C_6H_4\begin{cases} O.C_2H_5 \\ NH.CO.CH_3 \end{cases}}$$

Phenacetin forms small, colourless, glistening crystals, melting

at 135°. It is nearly insoluble in cold water, fairly soluble in boiling water and in alcohol, forming neutral solutions.

Acidum Picricum. *Picric Acid.* *Syns.* Carbazotic Acid; Trinitrophenol, $C_6H_2(NO_2)_3.OH$:



Picric acid.

This compound is formed by the action of nitric acid on many nitrogen-containing organic materials, such as wool, silk, or leather. It is prepared by dissolving phenol (20 grammes) in concentrated sulphuric acid (11·5 mils), and slowly adding the solution to cold concentrated nitric acid (60 mils). When the first reaction is over, the mixture is heated on a water-bath for two hours. On cooling, a mass of picric acid crystals separates. A little water is added, and the crystals are filtered off and recrystallised from boiling water.

Picric acid is a bright yellow crystalline powder, melting at 122°. It is soluble 1-90 in water and 1-10 in alcohol (90 per cent), forming solutions which stain the skin yellow. It has an intensely bitter taste.

Picric acid has strong acid properties, owing to the effect of the nuclear $-NO_2$ groups on the phenolic hydroxyl group. It is acid to phenolphthalein and decomposes metallic carbonates, forming well-defined crystalline salts. Many of the pitrates, such as potassium picrate, $C_6H_2(NO_2)_3.OK$, and ammonium picrate, $C_6H_2(NO_2)_3.ONH_4$, explode violently on percussion or if rapidly heated.

Quantitative Estimation.—Acidum Picricum is required to contain not less than 99 per cent of trinitrophenol, $C_6H_2(NO_2)_3.OH$. Weigh about 0·5 gramme, dissolve in hot water, and titrate with N/10 sodium hydroxide, using phenolphthalein as indicator:

$$NaOH + C_6H_2(NO_2)_3.OH = C_6H_2(NO_2)_3.ONa + H_2O,$$
$$NaOH \equiv C_6H_2(NO_2)_3.OH,$$
$$40 \equiv 229,$$
$$1000 \text{ mils N/1 NaOH} \equiv 229 \text{ grammes of } C_6H_2(NO_2)_3.OH,$$
$$1 \text{ mil N/10 NaOH} \equiv \cdot 0229 \text{ gramme of } C_6H_2(NO_2)_3.OH.$$

HOMOLOGUES OF PHENOL

There are three compounds of the formula $C_6H_4(CH_3).OH$, namely, *o*-, *m*-, and *p-cresols*. The o- and p-compounds are deliquescent crystalline solids, very similar to phenol, but m-cresol is a liquid.

The cresols can be prepared by methods similar to those described for the preparation of phenol. Thus the potassium salt of a toluene sulphonic acid can be fused with potassium hydroxide :

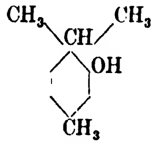
$$C_6H_4(CH_3).SO_3K + KOH = C_6H_4(CH_3).OH + K_2SO_3,$$

Potassium o-, m-, or p-toluene sulphonate. — o-, m-, or p-cresol.

or a diazotised solution of the corresponding toluidine may be boiled with water.

Cresol, *Cresol,* is a mixture of the three isomers, and is obtained from coal-tar. It is a pale yellowish-brown liquid, which darkens on keeping. Its specific gravity should lie between 1·04 and 1·05, and at least 90 per cent should distil between 195° and 205°. It is soluble 1-50 in water, freely in glycerin, alcohol, ether, and chloroform. The aqueous solution is neutral to litmus, and gives, on treatment with ferric chloride, a transient blue colour.

Thymol, *Thymol,* is a phenol which occurs in the volatile oil of *Thymus vulgaris,* and constitutes 40 per cent of Oleum Ajowan. It is 1-hydroxy-3-methyl-6-isopropyl-benzene, and its constitutional formula is :

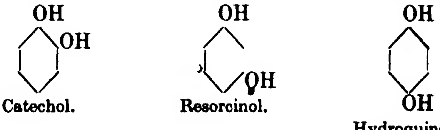


Thymol.

Thymol forms large, colourless crystals, melting at 50°-51°, and has a characteristic odour.

Dihydric Phenols

There are three isomeric dihydroxy-benzenes, namely :



Catechol. Resorcinol. Hydroquinone (quinol).

They are all colourless crystalline compounds, and are more readily soluble in water than the monohydric phenols. Chemically they differ from the monohydric phenols in being powerful reducing agents.

Catechol, o-dihydroxy-benzene, $C_6H_4(OH)_2$, was first obtained

by dry distillation of catechu. It can be prepared from guaiacol by heating it with concentrated hydriodic acid:

$$\underset{\text{Guaiacol.}}{C_6H_4(O.CH_3).OH} + HI = C_6H_4(OH)_2 + CH_3I.$$

Catechol forms colourless crystals, melting at 104°. Its aqueous solution gives, with ferric chloride, a green coloration.

Guaiacol, *Guaiacol*, methyl catechol, $C_6H_4(O.CH_3).OH$, is manufactured by the fractional distillation of beech-tar creosote. It is also made synthetically by heating a mixture of equimolecular proportions of catechol, potassium hydroxide, and potassium methyl sulphate in a closed vessel at 170°-180°:

$$C_6H_4(OH)_2 + KOH + CH_3.KSO_4 = C_6H_4(O.CH_3).OH + K_2SO_4 + H_2O.$$

When pure, guaiacol forms large colourless crystals, melting at 28°, but it is often met with as a colourless liquid. It has a characteristic tarry odour, and is soluble 1-80 in water, freely in alcohol and ether.

Since guaiacol contains one —OH group, it behaves as a monohydric phenol. Thus it dissolves in aqueous sodium hydroxide, forming a mono-sodium derivative, $C_6H_4(O.CH_3).ONa$.

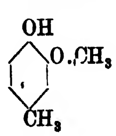
On adding very dilute ferric chloride solution, drop by drop, to an alcoholic solution of guaiacol, a blue coloration is produced, changing, on addition of more ferric chloride, to green, and finally to yellow.

Guaiacol Carbonas, *Guaiacol Carbonate*, $[C_6H_4(O.CH_3).O]_2CO$, is prepared by the action of carbonyl chloride on the sodium salt of guaiacol:

$$2C_6H_4(O.CH_3).ONa + COCl_2 = \begin{array}{l} C_6H_4(O.CH_3).O \\ C_6H_4(O.CH_3).O \end{array}\!\!\!> CO + 2NaCl.$$

It is a neutral crystalline compound, melting at 85° to 88°, and is insoluble in water. Boiling dilute sodium hydroxide hydrolyses it to sodium carbonate and the sodium derivative of guaiacol.

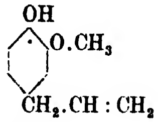
Creosol is a homologue of guaiacol, and has the constitutional formula



It occurs in Pix Liquida and other varieties of wood tar, and is one of the two main constituents of Creosotum (the other being guaiacol).

Creosol is an oily liquid, and is very similar to guaiacol in chemical properties. With ferric chloride it gives a green coloration.

Eugenol is a compound closely related to guaiacol, but containing an unsaturated side-chain :

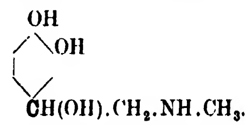


Eugenol.

Eugenol constitutes about 85-90 per cent of Oleum Caryophylli, and also occurs, in small quantities, in Oleum Cinnamomi and certain other essential oils.

Eugenol is a colourless oil, with an odour of cloves. Being a phenol, it gives a blue colour with ferric chloride (in alcoholic solution), and dissolves freely in solutions of potassium hydroxide ; on this latter fact depends the pharmacopœial method for the estimation of eugenol in Oleum Caryophylli.

Adrenalinum, *Adrenalin*, obtained from the suprarenal glands of animals, is a derivative of catechol of the formula



Adrenalin is a nearly white microcrystalline powder, and is only very sparingly soluble in water and in the common organic solvents It is a secondary base, and combines with dilute mineral acids with formation of soluble salts. The molecule contains an asymmetric carbon atom, shown in heavy type, and the naturally occurring substance is lævo-rotatory.

Resorcinum, *Resorcin, Syn.* Resorcinol, $C_6H_4(OH)_2$, is manufactured by fusing sodium benzene m-disulphonate, $C_6H_4(SO_3Na)_2$ with sodium hydroxide, a reaction analogous to that described for the preparation of phenol (Method 2) :

$$C_6H_4(SO_3Na)_2 + 4NaOH = C_6H_4(ONa)_2 + 2Na_2SO_3 + 2H_2O.$$

Resorcinol forms colourless crystals, with a faint odour, melting at 110°-111°. It dissolves freely in water, alcohol, and ether. Its alkaline solutions darken on exposure to air, owing to atmospheric oxidation, this being a characteristic of many polyhydric phenols. Its neutral aqueous solution gives, with ferric chloride, a bluish-violet colour.

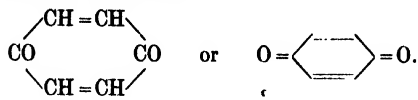
Hydroquinone, quinol, $C_6H_4(OH)_2$, is formed as a product of hydrolysis of the glucoside arbutin (p. 383). It forms colourless crystals, melting at 169°. It is readily soluble in water, and its aqueous solution, on warming with ferric chloride, gives an odour of quinone.

Quinone, $C_6H_4O_2$, is formed when quinol is treated with mild

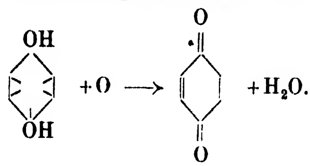
oxidising agents, such as ferric chloride. It is generally prepared by oxidising aniline with potassium dichromate and dilute sulphuric acid.

Quinone forms yellow needles, with a very penetrating and characteristic odour, melting at 116°. It sublimes when heated, and is volatile in steam. It is sparingly soluble in water, and has none of the properties of a phenol.

Quinone has the constitution :



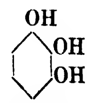
As can be seen, it is an unsaturated diketone, and is very different in structure from the ordinary aromatic ring compounds. Its formation from quinol can be represented as follows :



Being an unsaturated compound, quinone can combine with two or four atoms of a halogen. When treated with bromine, for example, it yields first a dibromide, $C_6H_4O_2Br_2$, and finally a tetrabromide, $C_6K_4O_2Br_4$. On reduction with sulphurous acid it is converted into hydroquinone.

TRIHYDRIC PHENOLS

Pyrogallol, pyrogallic acid, $C_6H_3(OH)_3$, is 1, 2, 3-trihydroxybenzene :



Pyrogallol.

It is formed when gallic acid is gently heated :

$$\underset{\text{Gallic acid.}}{C_6H_2(OH)_3.COOH} = C_6H_3(OH)_3 + CO_2.$$

Pyrogallol is a colourless crystalline compound, melting at 115°, and is readily soluble in water. Like the dihydric phenols, it is a powerful reducing agent, and its alkaline solutions rapidly turn brown on exposure to air owing to atmospheric oxidation. It precipitates metallic silver from solutions of silver salts, and on this account is employed as a developer in photography, as are also hydroquinone and certain other phenolic compounds.

CHAPTER XXXIII

AROMATIC ALCOHOLS, ALDEHYDES, AND KETONES

ALCOHOLS

It has been pointed out (p. 334) that the chemical behaviour of a particular radicle in the molecule of an aromatic compound depends largely on whether the radicle is directly attached to a carbon atom of a side-chain or of the nucleus. Radicles in a side-chain behave, as a rule, in much the same way as they do when present in an aliphatic compound; radicles in the nucleus, on the other hand, show entirely different properties. These general statements are well illustrated by a study of the aromatic hydroxy compounds. Compounds with hydroxyl groups in the nucleus have the properties characteristic of phenols, and have little in common with the aliphatic alcohols; those with hydroxyl groups in the side-chain, on the other hand, resemble the aliphatic alcohols in nearly all their chemical properties.

Benzyl alcohol, $C_6H_5.CH_2.OH$, is isomeric with the cresols. It occurs, in the form of its benzoic and cinnamic esters, in Balsamum Peruvianum, and to a smaller extent in Balsamum Tolutanum. It can be prepared by hydrolysing benzyl chloride with boiling alkali:

$$C_6H_5.CH_2Cl + KOH = C_6H_5.CH_2.OH + KCl.$$

It can also be prepared by reducing benzaldehyde with nascent hydrogen:

$$\underset{\text{Benz-aldehyde.}}{C_6H_5.CHO} + 2H = C_6H_5.CH_2.OH.$$

Both these methods are similar to those employed for the preparation of aliphatic alcohols. Benzyl alcohol can also be made by shaking benzaldehyde with aqueous potassium hydroxide, a method which has no analogue in the aliphatic series:

$$2C_6H_5.CHO + KOH = C_6H_5.CH_2.OH + \underset{\text{Potassium benzoate.}}{C_6H_5.COOK}.$$

Benzyl alcohol is a colourless liquid, with an odour recalling that of almonds. It boils at 206°, and is sparingly soluble in water.

In chemical properties benzyl alcohol closely resembles the primary aliphatic alcohols. It is acted on by sodium and potassium with evolution of hydrogen and formation of metallic derivatives, such as $C_6H_5.CH_2.ONa$. These derivatives, unlike the metallic derivatives of phenols, are immediately decomposed by water, with regeneration of benzyl alcohol. Halides of phosphorus convert benzyl alcohol into the corresponding benzyl halide. For example:

$$C_6H_5.CH_2.OH + PCl_5 = C_6H_5.CH_2Cl + POCl_3 + HCl.$$

Benzyl alcohol reacts with acids in the absence of water, forming esters, such as benzyl acetate, $CH_3.COOCH_2.C_6H_5$.

On oxidation with dilute nitric acid benzyl alcohol is converted first into benzaldehyde and then into benzoic acid:

$$C_6H_5.CH_2.OH + O = C_6H_5.CHO + H_2O,$$
$$C_6H_5.CHO + O = C_6H_5.COOH.$$

Saligenin, salicyl alcohol, o-hydroxy-benzyl alcohol, $C_6H_4(OH).CH_2.OH$, occurs, in combination, in the glucoside salicin, from which it can be obtained by hydrolysis. It forms colourless crystals, melting at 82°, and is readily soluble in water.

Saligenin is both a phenol and an alcohol. As a phenol it forms a mono-sodium derivative, $C_6H_4(ONa).CH_2.OH$, when treated with sodium hydroxide in aqueous solution, and its aqueous solution gives with ferric chloride a blue colour. As an alcohol it forms a di-sodium derivative, $C_6H_4(ONa).CH_2.ONa$, when treated with metallic sodium, and it can be oxidised first to salicylaldehyde and then to salicylic acid:

$$C_6H_4(OH).CH_2.OH + O = \underset{\text{Salicyl-aldehyde.}}{C_6H_4(OH).CHO} + H_2O,$$

$$C_6H_4(OH).CHO + O = \underset{\text{Salicylic acid.}}{C_6H_4(OH).COOH}.$$

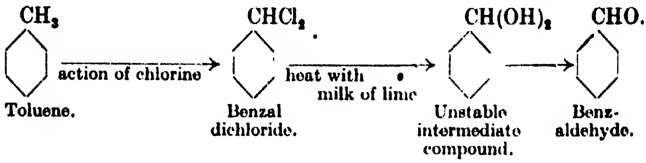
Aldehydes

Benzaldehyde, $C_6H_5.CHO$, occurs in the glucoside amygdalin, from which it is liberated on hydrolysis. It is formed when benzyl alcohol is oxidised, and when a mixture of calcium benzoate and calcium formate is strongly heated (compare the preparation of acetaldehyde, p. 235):

$$\underset{\text{Calcium benzoate.}}{(C_6H_5.COO)_2Ca} + (H.COO)_2Ca = 2C_6H_5.CHO + 2CaCO_3.$$

It is manufactured by converting toluene into benzal dichloride (p. 334), and hydrolysing the product with hot milk of lime. The

first product of hydrolysis is an unstable dihydroxy compound, which immediately loses a molecule of water, forming benzaldehyde :



Benzaldehyde is a colourless oil, boiling at 179°, and has an odour of bitter almonds. It is only sparingly soluble in water, but is miscible with alcohol. It yields benzyl alcohol on reduction with nascent hydrogen, and on exposure to air it is slowly oxidised to benzoic acid. Like the aliphatic aldehydes, it forms a bisulphite compound, a hydrazone, an oxime, and a cyanohydrin.

$$\underset{\text{Benzyl alcohol.}}{C_6H_5.CH_2.OH} \xleftarrow{\text{reduction}} C_6H_5.CHO \xrightarrow{\text{oxidation}} \underset{\text{Benzoic acid.}}{C_6H_5.COOH}$$

$$C_6H_5.CHO \xrightarrow{NaHSO_3} \underset{\text{Benzaldehyde sodium bisulphite.}}{C_6H_5.CH(OH).SO_3Na}$$

$$C_6H_5.CHO \xrightarrow{C_6H_5.NH.NH_2} \underset{\text{Benzaldehyde hydrazone.}}{C_6H_5.CH:N.NH.C_6H_5}$$

$$C_6H_5.CHO \xrightarrow{NH_2.OH} \underset{\text{Benzaldoxime.}}{C_6H_5.CH:N.OH}$$

$$C_6H_5.CHO \xrightarrow{HCN} \underset{\text{Benzaldehyde cyanohydrin.}}{C_6H_5.CH(OH).CN}$$

Mention has already been made (p. 355) of the curious reaction by which benzaldehyde, on treatment with aqueous sodium or potassium hydroxide, yields benzyl alcohol and a salt of benzoic acid.

Salicylaldehyde, o-hydroxy-benzaldehyde, $C_6H_4(OH).CHO$, is formed when saligenin is oxidised with potassium dichromate and dilute sulphuric acid. It can be made synthetically by boiling a solution of phenol in aqueous sodium hydroxide with chloroform (reaction of Reimer and Tiemann) :

$$C_6H_5.OH + 4KOH + CHCl_3 = C_6H_4(OK).CHO + 3KCl + 3H_2O.$$

Salicylaldehyde is a colourless, oily liquid, with an odour of meadow-sweet, and boils at 196°. It is sparingly soluble in water.

Salicylaldehyde is both a phenol and an aldehyde. Its aqueous solution gives a violet colour on addition of ferric chloride, and,

though only sparingly soluble in water, it dissolves readily in aqueous sodium hydroxide, with formation of a sodium derivative, $C_6H_4(ONa).CHO$. It is converted by reducing agents into saligenin, and by oxidising agents into salicylic acid.

Cinnamic aldehyde, $C_6H_5.CH:CH.CHO$, is an unsaturated aromatic aldehyde, which occurs to the extent of 55-65 per cent in Oleum Cinnamomi. It can be prepared synthetically by heating the calcium salt of cinnamic acid with calcium formate :

$$\underset{\text{Calcium cinnamate.}}{(C_6H_5.CH:CH.COO)_2Ca} + (H.COO)_2Ca = 2C_6H_5.CH:CH.CHO + 2CaCO_3.$$

Cinnamic aldehyde is an oily liquid, boiling at 247°, and has the characteristic odour of cinnamon. On exposure to air it is slowly oxidised to cinnamic acid (p. 368).

KETONES

The aromatic ketones are not of great importance. They may contain either two aryl groups or one aryl and one alkyl.

Acetophenone, methyl phenyl ketone, $C_6H_5.CO.CH_3$, can be prepared by heating a mixture of calcium acetate and calcium benzoate, a method analogous to that employed for the preparation of aliphatic ketones (p. 241) :

$$(CH_3.COO)_2Ca + (C_6H_5.COO)_2Ca = 2C_6H_5.CO.CH_3 + 2CaCO_3.$$

It is generally made, by a modification of Friedel and Crafts' reaction (p. 330), by the action of acetyl chloride on benzene in presence of anhydrous aluminium chloride :

$$C_6H_6 + CH_3.COCl = C_6H_5.CO.CH_3 + HCl.$$

Acetophenone is a colourless crystalline compound, melting at 20°. In chemical properties it closely resembles the aliphatic ketones. It yields a hydrazone and an oxime, and on reduction it is converted into the secondary alcohol, $C_6H_5.CH(OH).CH_3$.

Benzophenone, diphenyl ketone, $(C_6H_5)_2CO$, can be prepared by methods analogous to those described for acetophenone, namely, by heating calcium benzoate alone, or by the action of benzoyl chloride on benzene in presence of anhydrous aluminium chloride :

$$(C_6H_5.COO)_2Ca = C_6H_5.CO.C_6H_5 + CaCO_3,$$
$$C_6H_6 + \underset{\substack{\text{Benzoyl}\\ \text{chloride.}}}{C_6H_5.COCl} = C_6H_5.CO.C_6H_5 + HCl.$$

Benzophenone is a crystalline solid, very similar in chemical properties to acetophenone.

CHAPTER XXXIV

THE AROMATIC CARBOXYLIC ACIDS

THE aromatic carboxylic acids are generally prepared by methods similar to those employed for the preparation of the corresponding aliphatic compounds. Several of them are used in pharmacy, both in the free state and in the form of their metallic salts and esters.

BENZOIC ACID, $C_6H_5 . COOH$

Benzoic acid occurs as its benzyl ester in Balsamum Peruvianum, and to a smaller extent in Balsamum Tolutanum. Benzoinum contains about 6·5 per cent of free benzoic acid, together with smaller quantities of benzoic esters.

Preparation.—(1) Benzoic acid is sometimes obtained from Benzoinum, or from unofficial varieties of benzoin, by heating the resin in iron vessels, when the benzoic acid sublimes. The sublimate is purified by recrystallisation from boiling water.

(2) It can be prepared by oxidising benzyl alcohol or benzaldehyde, or by hydrolysing phenyl cyanide, all these methods being similar to those previously described for the preparation of the fatty acids :

$$C_6H_5.CH_2.OH \longrightarrow C_6H_5.CHO \longrightarrow C_6H_5.COOH,$$
$$C_6H_5.CN + 2H_2O = C_6H_5.COOH + NH_3.$$

(3) Boiling acidified potassium permanganate slowly oxidises toluene to benzoic acid :

$$C_6H_5.CH_3 + 3O = C_6H_5.COOH + H_2O.$$

As has been previously mentioned (p. 331), not only toluene, but all homologues of benzene containing a single side-chain yield benzoic acid on oxidation.

(4) Benzoic acid is formed when benzo-trichloride is hydrolysed, a method analogous to the preparation of benzaldehyde from benzal dichloride (p. 357) :

$$\underset{\text{Benzo-trichloride.}}{C_6H_5.CCl_3} \longrightarrow \underset{\text{Unstable intermediate compound.}}{C_6H_5.C(OH)_3} \longrightarrow C_6H_5.COOH.$$

(5) Benzoic acid is manufactured from toluene. In one process the toluene is first converted into benzyl chloride, and this is then converted into benzoic acid by oxidation with nitric acid:

$$C_6H_5.CH_2Cl + 2O = C_6H_5.COOH + HCl.$$

Properties.—Benzoic acid crystallises in light, colourless, glistening plates. It is sparingly soluble in cold water, readily in hot, and is volatile in steam.

In chemical properties it closely resembles the fatty acids. Its hot aqueous solution dissolves metallic carbonates with effervescence, forming the corresponding benzoates. Ferric benzoate is formed as a buff-coloured precipitate when ferric chloride is added to a neutral solution of a soluble benzoate.

The following benzoates are official:

Ammonii Benzoas, $C_6H_5.COONH_4$ (p. 97).
Sodii Benzoas, $C_6H_5.COONa$ (p. 85).

Tests for Benzoates.—(1) When heated alone benzoates char. If heated with powdered soda-lime they evolve vapours with an odour of benzene:

$$C_6H_5.COONa + NaOH = C_6H_6 + Na_2CO_3.$$

(2) If a fairly concentrated neutral solution of a benzoate be treated with dilute hydrochloric acid a white precipitate of benzoic acid is produced.

(3) Ferric chloride, added to a neutral solution of a benzoate, gives a buff-coloured precipitate of ferric benzoate (distinction from salicylate).

(4) If a benzoate is warmed with a mixture of alcohol and concentrated sulphuric acid, the characteristic odour of ethyl benzoate (p. 361) will be noticed.

ACIDUM BENZOICUM

Benzoic Acid

The official substance crystallises in light, feathery plates and needles, soluble 1-450 in water, 1-3 in alcohol, 1-2·5 in ether, and 1-7 in chloroform. If prepared synthetically from toluene it is odourless, and melts at 121·5°, but if obtained by sublimation from benzoin it has an agreeable, aromatic odour, and melts at about 120°.

Tests for Impurities. *Non-volatile Matter.*—When heated in a dry tube it should melt and sublime, leaving no more than a slight residue.

Oxalate.—Boil with dilute acetic acid, cool thoroughly, filter, dilute the filtrate to about twice its bulk, and add calcium chloride. There should be no white precipitate of calcium oxalate.

Chlorobenzoic Acid, $C_6H_4Cl.COOH$.—Mix about 0·5 gramme of

the sample with about twice its weight of calcium carbonate, and heat the mixture to redness in a crucible. Any chlorobenzoic acid will be decomposed with formation of calcium chloride. Allow the mass to cool, add excess of dilute nitric acid, boil, filter, and add to the filtrate silver nitrate. No more than a slight opalescence should be produced.

Cinnamic Acid (p. 368).—Warm about 0·5 gramme with an equal quantity of potassium permanganate and about 5 mils of dilute sulphuric acid. No odour of benzaldehyde should be noticeable.

Arsenic Limit.—2 parts per million (p. 176).

DERIVATIVES OF BENZOIC ACID

Numerous compounds can be prepared from benzoic acid by the action of various reagents, usually by methods similar to those employed in the aliphatic series. Only the more important of these derivatives will be described.

Benzoyl chloride, $C_6H_5.COCl$, bears the same relationship to benzoic acid as acetyl chloride does to acetic acid. It is prepared by the action of phosphorus pentachloride on benzoic acid :

$$C_6H_5.COOH + PCl_5 = C_6H_5.COCl + POCl_3 + HCl.$$

It is a fuming liquid, boiling at 198°, and is hydrolysed to benzoic acid by hot water :

$$C_6H_5.COCl + H_2O = C_6H_5.COOH + HCl.$$

Benzoic anhydride, $(C_6H_5.CO)_2O$, is formed when sodium benzoate is treated with benzoyl chloride :

$$C_6H_5.COONa + C_6H_5.COCl = \begin{matrix} C_6H_5.CO \\ C_6H_5.CO \end{matrix}\!\!>\!O + NaCl.$$

It is a colourless, crystalline compound, melting at 42°.

Ethyl benzoate, $C_6H_5.COOC_2H_5$, is formed when ethyl alcohol is treated with benzoyl chloride, but it is usually prepared by heating a mixture of ethyl alcohol, benzoic acid, and concentrated sulphuric acid :

$$C_6H_5.COOH + C_2H_5.OH = C_6H_5.COOC_2H_5 + H_2O.$$

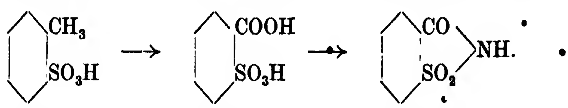
It is a colourless liquid, boiling at 213°, and has a pleasant aromatic odour.

Benzamide, $C_6H_5.CO.NH_2$, is prepared by shaking ethyl benzoate with a concentrated solution of ammonium hydroxide :

$$C_6H_5.COOC_2H_5 + NH_3 = C_6H_5.CO.NH_2 + C_2H_5.OH.$$

It forms colourless crystals, melting at 130°. On boiling with aqueous alkalies it is hydrolysed, with evolution of ammonia.

Glusidum, *Gluside,* $C_6H_4\left\langle\begin{matrix}CO\\SO_2\end{matrix}\right\rangle NH$, known in commerce as saccharin, is an important derivative of benzoic acid. It is prepared synthetically from toluene. When heated with concentrated sulphuric acid toluene is converted into toluene o-sulphonic acid, together with smaller quantities of toluene p-sulphonic acid. The ortho acid is oxidised by potassium permanganate to o-sulpho-benzoic acid, and this, on treatment with ammonia, yields gluside :

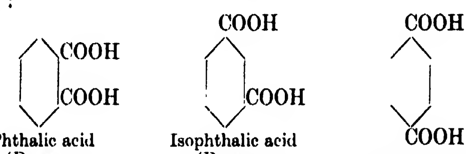


Toluene o-sulphonic acid. — o-Sulpho-benzoic acid. — Gluside (Imide of o-sulpho-benzoic acid).

Gluside is a white crystalline powder, sparingly soluble in water. It dissolves readily in aqueous sodium hydroxide or carbonate, with formation of a sodium salt, $C_6H_4\left\langle\begin{matrix}CO\\SO_2\end{matrix}\right\rangle NNa$, known as "soluble gluside".

THE PHTHALIC ACIDS

There are three isomeric dicarboxylic acids derived from benzene, namely :



Phthalic acid (Benzene o-dicarboxylic acid). — Isophthalic acid (Benzene m-dicarboxylic acid). — Terephthalic acid (Benzene p-dicarboxylic acid).

Of these phthalic acid is the most important.

Phthalic acid, $C_6H_4(COOH)_2$, is formed when o-xylene is oxidised with acid permanganate :

$$C_6H_4(CH_3)_2 + 6O = C_6H_4(COOH)_2 + 2H_2O.$$

It is prepared by oxidising the hydrocarbon naphthalene (p. 370) with sulphuric acid, in the presence of a little mercury as catalyst :

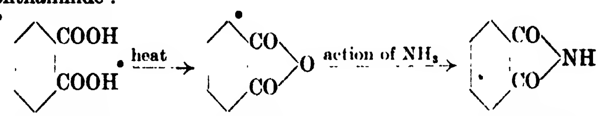
$$C_{10}H_8 + 9O = C_6H_4(COOH)_2 + 2CO_2 + H_2O.$$

Phthalic acid forms colourless crystals, melting at 184°, and is sparingly soluble in cold water. In most chemical properties it

closely resembles benzoic acid. On heating with soda-lime it is converted into benzene :

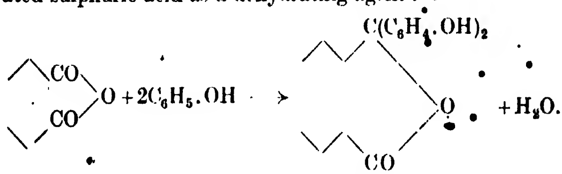
$$C_6H_4(COOH)_2 + 4NaOH = C_6H_6 + 2Na_2CO_3 + 2H_2O.$$

Phthalic anhydride, $C_6H_4\left\langle{CO \atop CO}\right\rangle O$, a compound similar in constitution to succinic anhydride (p. 287), is formed as a sublimate of long, colourless needles when phthalic acid is strongly heated. Phthalic anhydride is converted, by the action of ammonia, into phthalimide :



Phthalic acid. Phthalic anhydride. Phthalimide.

Phenolphthaleinum, *Phenolphthalein*, $C_{20}H_{14}O_4$, is prepared by heating phthalic anhydride with phenol, in the presence of concentrated sulphuric acid as a dehydrating agent :



Phenolphthalein.

Phenolphthalein is a white crystalline powder, almost insoluble in water, but easily soluble in alcohol. A very dilute solution in aqueous alcohol is employed in volumetric analysis as an indicator, its use depending on the fact that phenolphthalein reacts with alkalies, with formation of intensely red salts.

Salicylic Acid, $C_6H_4(OH).COOH$

Salicylic, or o-hydroxybenzoic acid, is the acid corresponding to saligenin (p. 356) and salicylaldehyde (p. 357). It occurs naturally in Oleum Gaultheriæ, which consists almost entirely of methyl salicylate, $C_6H_4(OH).COOCH_3$.

Preparation.—(1) Salicylic acid is formed when saligenin or salicylaldehyde is oxidised :

$$C_6H_4(OH).CH_2.OH \longrightarrow C_6H_4(OH).CHO \longrightarrow C_6H_4(OH).COOH.$$

(2) It is formed when a solution of phenol in aqueous sodium hydroxide is heated with carbon tetrachloride under pressure, this

being analogous to the Reimer-Tiemann method for the preparation of salicylaldehyde (p. 357):

$$C_6H_5ONa + CCl_4 + 5NaOH = C_6H_4(ONa).COONa + 4NaCl + 3H_2O.$$

(3) For pharmaceutical purposes it is sometimes prepared by boiling oil of wintergreen (methyl salicylate) with dilute potassium hydroxide, when the oil is hydrolysed, with formation of methyl alcohol and the potassium salt of salicylic acid:

$$C_6H_4(OH).COOCH_3 + 2KOH = C_6H_4(OK).COOK + CH_3.OH + H_2O.$$

The methyl alcohol is distilled off, and the residual solution is concentrated by evaporation, cooled, and acidified with hydrochloric acid, when free salicylic acid is precipitated. The crude product is purified by recrystallisation from hot water.

(4) Salicylic acid is manufactured by Kolbe's process. Dry sodium phenate is saturated with carbon dioxide under pressure, when sodium phenyl carbonate is formed:

$$C_6H_5.ONa + CO_2 = \underset{\text{Sodium phenyl carbonate.}}{CO\left<\begin{matrix}ONa\\O.C_6H_5\end{matrix}\right.}$$

The product is heated at 130° under pressure, when it undergoes isomeric change to form sodium salicylicate:

$$CO\left<\begin{matrix}ONa\\O.C_6H_5\end{matrix}\right. \longrightarrow \underset{\text{Sodium salicylate.}}{C_6H_4(OH).COONa}$$

From the sodium salt the free acid is obtained by dissolving in water and adding hydrochloric acid.

The acid made by Kolbe's process is known as "artificial" or "synthetic" salicylic acid, as distinct from the "natural" acid prepared from oil of wintergreen.

Properties.—Salicylic acid forms small colourless, prismatic crystals, which melt at 156°, and when strongly heated sublime, with partial decomposition. When heated with lime it decomposes with formation of calcium carbonate and phenate:

$$2C_6H_4(OH).COOH + 3CaO = (C_6H_5.O)_2Ca + 2CaCO_3 + H_2O.$$

Salicylic acid has the properties of both an acid and a phenol. It is sparingly soluble in cold water, but dissolves readily in solutions of alkali carbonates, with formation of mono-metallic salts, such as *sodium salicylate*, $C_6H_4(OH).COONa$. When treated with excess of sodium or potassium hydroxide the hydrogen atoms of both the acidic and the phenolic hydroxyl groups are displaced by the metal, with formation of a di-metallic salt, such as *disodium salicylate*, $C_6H_4(ONa).COONa$. These di-metallic salts are decomposed by

carbon dioxide, with formation of the mono-metallic salts. For example :

$$2C_6H_4(ONa).COONa + CO_2 + H_2O = 2C_6H_4(OH).COONa + Na_2CO_3.$$

The following metallic salicylates are official, and have been previously described :

Bismuthi Salicylas, $C_6H_4(OH).COO(BiO)$ (p. 154).
Sodii Salicylas, $C_6H_4(OH).COONa$ (p. 86).

Tests for Salicylates.—(1) When heated they char, evolving inflammable vapours with an odour of phenol.

(2) When hydrochloric acid is added to a concentrated aqueous solution of a salicylate, a white precipitate of salicylic acid is produced.

(3) Ferric chloride, added to a neutral solution of a salicylate, gives a violet colour.

(4) When warmed with a few drops of alcohol and concentrated sulphuric acid, an odour recalling that of oil of wintergreen is evolved.

ACIDUM SALICYLICUM

Salicylic Acid

The official substance crystallises in distinct colourless prisms, having a sweetish acid taste. Soluble about 1-500 in water, 1-3·5 in alcohol (90 per cent), and 1-2 in ether. Its melting-point is 156°-157°.

Tests for Impurities. *Metallic Compounds.*—On strong ignition in an open crucible it should leave no appreciable ash.

Iron, Organic Impurities, and Colouring Matter.—Shake with a little water, filter, and evaporate the filtrate to dryness on a water-bath. The residue should be white, and should have no buff-tinted fringe.

Readily carbonisable Organic Impurities.—A solution in cold concentrated sulphuric acid should not acquire more than a faint brownish tint in fifteen minutes.

Phenol.—Dissolve about a gramme in cold aqueous sodium carbonate, shake the solution with an equal volume of ether, and allow the ether layer to evaporate spontaneously. The residue, if any, should be free from the odour of phenol.

Arsenic Limit.—2 parts per million (p. 176).

Derivatives of Salicylic Acid

Methyl Salicylas, *Methyl Salicylate,* $C_6H_4(OH).COOCH_3$, is prepared by distilling a mixture of salicylic acid, methyl alcohol, and concentrated sulphuric acid :

$$C_6H_4(OH).COOH + CH_3.OH = C_6H_4(OH).COOCH_3 + H_2O.$$

Methyl salicylate is a colourless, oily liquid, boiling at 220°, and is

only very sparingly soluble in water. Its molecule still contains the phenolic —OH group, and on this account it dissolves freely in solutions of alkali hydroxides to form metallic derivatives, such as *sodium methyl salicylate*, $C_6H_4(ONa).COOCH_3$. These metallic derivatives react with dry alkyl halides, with formation of compounds of the ether type, such as *methyl methylsalicylate*, $C_6H_4(O.CH_3).COOCH_3$. Methyl methylsalicylate, when boiled with dilute alkalies, is hydrolysed with formation of an alkali salt of *methylsalicylic acid*, $C_6H_4(O.CH_3).COOH$; the second methyl group is very firmly held, and cannot be removed by hydrolysis.

Methyl salicylate constitutes about 99 per cent of Oleum Gaultheriæ, and the synthetic ester is frequently employed for purposes for which the oil was formerly used. The two can be distinguished by their odours, which are slightly different, owing to the presence of traces of other compounds in the natural product.

Salol, *Salol*, phenyl salicylate, $C_6H_4(OH).COOC_6H_5$, is prepared by the action of phosphorus oxychloride on a mixture of sodium salicylate and sodium phenate:

$$2C_6H_4(OH).COONa + 2C_6H_5ONa + POCl_3 \\ = 2C_6H_4(OH).COOC_6H_5 + 3NaCl + NaPO_3.$$

Salol is a crystalline powder with a characteristic aromatic odour, melting at 42°-43°. It is almost insoluble in water, but dissolves readily in organic solvents, forming neutral solutions. When boiled with dilute alkalies it undergoes hydrolysis:

$$C_6H_4(OH).COOC_6H_5 + 3NaOH \\ = C_6H_4(ONa).COONa + C_6H_5.ONa + 2H_2O.$$

Tests for Impurities.—When shaken with water and filtered, separate portions of the filtrate should give no coloration with dilute ferric chloride solution (absence of phenol, salicylic acid, and readily soluble salicylates), no opalescence with dilute nitric acid and silver nitrate (absence of chloride), and no turbidity with dilute hydrochloric acid and barium chloride (absence of sulphate).

On ignition, salol should leave no appreciable ash.

Acidum Acetylsalicylicum, *Acetylsalicylic Acid*, $C_6H_4(O.CO.CH_3).COOH$, popularly known as "aspirin", is prepared by the action of acetyl chloride or acetic anhydride on salicylic acid:

$$C_6H_4(OH).COOH + CH_3.COCl = C_6H_4(O.CO.CH_3).COOH + HCl.$$

It is a white crystalline powder, with a slightly acid taste, and is sparingly soluble in water. Melting-point, 133°-135°. Boiling dilute alkalies hydrolyse it, with formation of salts of acetic and salicylic acids.

Tests for Impurities.—When 0·5 gramme is shaken with 20 mils of water and a few drops of very dilute ferric chloride solution is added, no violet coloration should be produced (absence of salicylic acid).

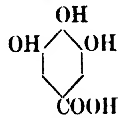
On ignition, it should leave no appreciable ash.

Lead Limit.—10 parts per million (p. 173).

Arsenic Limit.—2 parts per million (p. 176).

OTHER AROMATIC ACIDS

Gallic Acid, $C_6H_2(OH)_3.COOH$.—Gallic acid occurs in the form of complex glucosides ("tannins", p. 386) in galls and other plant products. It is 3, 4, 5-trihydroxybenzoic acid :



Gallic acid.

It is prepared by hydrolysing tannic acid (p. 385) with boiling dilute sulphuric acid, but can also be obtained directly from galls. The powdered galls are boiled for half an hour with dilute sulphuric acid in order to hydrolyse the tannic acid, and the hot liquor is filtered through calico. Gallic acid crystallises from the filtrate on cooling, and can be purified by dissolving in hot water, decolorising with animal charcoal, and recrystallising.

Gallic acid crystallises in white silky needles, containing 1 molecule of water. It is soluble about 1-100 in cold water, the solubility increasing rapidly with rise in temperature.

When heated it loses its water of crystallisation at 100°, and at higher temperatures it evolves carbon dioxide, with formation of pyrogallol :

$$C_6H_2(OH)_3.COOH = C_6H_3(OH)_3 + CO_2.$$

Like pyrogallol, gallic acid is a powerful reducing agent, and precipitates gold and silver from solutions of their salts. Its aqueous solution yields with ferric chloride a bluish-black precipitate.

Gallic acid was official in the 1898 Pharmacopœia.

Mandelic Acid, $C_6H_5.CH(OH).COOH$.—Mandelic acid is an example of an aromatic hydroxy-carboxylic acid with both the —OH and the —COOH groups in the side chain.

It is prepared by combining benzaldehyde with hydrocyanic acid, when benzaldehyde cyanohydrin is produced ; this on hydrolysis yields mandelic acid :

$$C_6H_5.CHO + HCN = C_6H_5.CH\begin{cases} OH \\ CN \end{cases}$$

Benzaldehyde cyanohydrin.

$$C_6H_5.CH\begin{cases}OH\\CN\end{cases} + 2H_2O = C_6H_5.CH\begin{cases}OH\\COOH\end{cases} + NH_3.$$

Mandelic acid.

Mandelic acid is a crystalline solid, and resembles lactic acid in that it has the properties of both a carboxylic acid and a secondary alcohol. It differs from salicylic acid in that the —OH group, being in the side chain, is not phenolic; thus it gives no coloration with ferric chloride, and only yields a mono-sodium salt when dissolved in excess of aqueous sodium hydroxide.

Like lactic acid, mandelic acid contains an asymmetric carbon atom, and can be resolved into optically active forms.

Benzaldehyde cyanohydrin, or mandelo-nitrile, $C_6H_5.CH(OH).CN$, also contains an asymmetric carbon atom, and exists in optically isomeric forms. It is a product of hydrolysis of many naturally occurring cyanogenetic glucosides (p. 382), some of which yield the *d*-form, some the *l*-form, and others the *dl*-mixture.

Cinnamic Acid, $C_6H_5.CH:CH.COOH$.—Cinnamic acid is an example of an unsaturated aromatic acid, and is derived from acrylic acid (p. 257) by substitution of the group C_6H_5— for a hydrogen atom. It occurs in Styrax Præparatus to the extent of 20 per cent or more.

Cinnamic acid is slowly formed when cinnamic aldehyde is exposed to air:

$$C_6H_5.CH:CH.CHO + O = C_6H_5.CH:CH.COOH.$$

It is usually prepared from benzaldehyde by heating it with anhydrous sodium acetate in the presence of acetic anhydride (Perkin's reaction):

$$C_6H_5.CHO + CH_3.COONa = C_6H_5.CH:CH.COONa + H_2O.$$

Sodium cinnamate.

Cinnamic acid is a crystalline solid, sparingly soluble in cold water, fairly easily in hot. It shows the usual properties of an unsaturated acid (p. 257); thus, it reduces a cold alkaline solution of potassium permanganate, and forms additive products with nascent hydrogen, halogens, and halogen acids:

$$C_6H_5.CH:CH.COOH \xrightarrow{+2H} C_6H_5.CH_2.CH_2.COOH.$$

β-Phenyl propionic acid (Hydrocinnamic acid).

$$C_6H_5.CH:CH.COOH \xrightarrow{+HBr} C_6H_5.CHBr.CH_2.COOH$$

β-Phenyl-β-bromo-propionic acid.

$$C_6H_5.CH:CH.COOH \xrightarrow{+Br_2} C_6H_5.CHBr.CHBr.COOH$$

β-Phenyl-αβ-dibromo-propionic acid.

A warm, neutral or acid, solution of potassium permanganate oxidises cinnamic acid to benzaldehyde, a reaction which is used in testing for cinnamic acid as impurity in benzoic acid, and in distinguishing between Sumatra benzoin and unofficial varieties of benzoin which contain little or no cinnamic acid:

$$C_6H_5.CH:CH.COOH + 4O = C_6H_5.CHO + 2CO_2 + H_2O.$$

CHAPTER XXXV

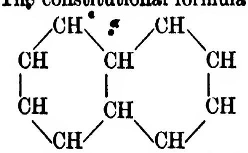
NAPHTHALENE, ANTHRACENE, PHENANTHRENE, AND THEIR DERIVATIVES

NAPHTHALENE, $C_{10}H_8$

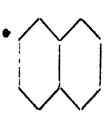
NAPHTHALENE is a hydrocarbon which occurs in coal-tar, from which source it is generally obtained. It crystallises in shining plates, melting at 79°, and has a peculiar and very characteristic odour.

Naphthalene closely resembles benzene in chemical properties. It is readily acted on by concentrated nitric and concentrated sulphuric acids, with formation of nitro-derivatives and sulphonic acids respectively. It is very stable towards most oxidising agents, but is readily oxidised to phthalic acid by sulphuric acid in the presence of metallic mercury as catalyst (p. 362).

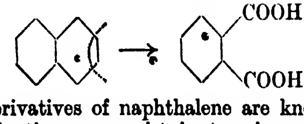
The constitutional formula of naphthalene is



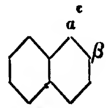
often contracted to



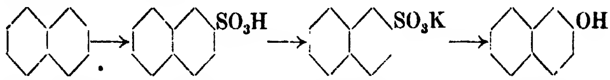
The molecule can thus be regarded as consisting of two benzene nucleii containing two carbon atoms in common. As in the case of benzene, the actual disposition of the fourth valency bonds of the carbon atoms is unknown. The formation of phthalic acid from naphthalene is due to the splitting up of one of the nucleii :



Numerous derivatives of naphthalene are known. The mono-substitution derivatives can exist in two isomeric forms, distinguished as α and β :



Naphthol, *β-Naphthol,* $C_{10}H_7.OH$.—From a pharmaceutical standpoint this is the most important derivative of naphthalene. It can be prepared from the hydrocarbon by heating it at 200° with concentrated sulphuric acid, converting the naphthalene β-sulphonic acid thus formed into its potassium salt, and then fusing this with potassium hydroxide :

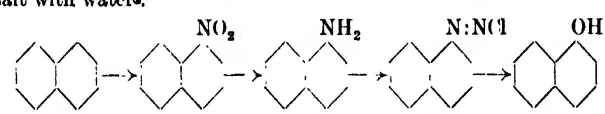


This is exactly analogous to the method by which phenol can be prepared from benzene (p. 346).

β-Naphthol is met with in small, colourless, crystalline plates, having a characteristic phenolic odour. Melting point, 122°. It is sparingly soluble in water, readily in alcohol and in ether, forming neutral solutions.

In chemical properties β-naphthol behaves like a phenol. Thus it dissolves freely in solutions of sodium or potassium hydroxides forming metallic derivatives, and is precipitated from these alkaline solutions by acids, or by the action of carbon dioxide. It can be distinguished from the α-compound by the fact that, when treated with ferric chloride in boiling aqueous solution, it gives a white precipitate, becoming brown.

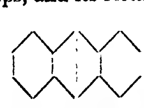
α-**Naphthol** can be prepared by converting naphthalene into α-nitronaphthalene by heating with concentrated nitric acid, reducing the product to α-naphthylamine by means of nascent hydrogen, and finally diazotising this base and boiling the diazonium salt with water:



α-Naphthol is a colourless crystalline compound, melting at 95°, and resembles the β-compound in its phenolic properties. Its aqueous solution gives, with ferric chloride, a violet precipitate.

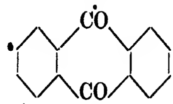
Anthracene, $C_{14}H_{10}$

Anthracene is a hydrocarbon obtained from coal-tar. Its molecule consists of two benzene nuclei joined together by two $>$CH groups, and its formula can therefore be written :

 or $C_6H_4\left\langle {CH \atop CH} \right\rangle C_6H_4$

Anthracene crystallises in colourless glistening plates, melting at 213°.

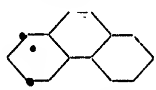
Anthraquinone, $C_{14}H_8O_2$.—When anthracene is heated with concentrated nitric acid it does not, as one might expect, yield a nitro-derivative, but is oxidised to anthraquinone, a compound of the formula



Anthraquinone forms yellow needles, melting at 285°, and has the usual properties of a ketone. In medicine anthraquinone is chiefly of interest on account of the fact that some of its derivatives are important constituents of the purgative drugs senna, aloes, rhubarb, and cascara (see p. 384).

PHENANTHRENE, $C_{14}H_{10}$

Phenanthrene is a hydrocarbon, isomeric with anthracene, which occurs in coal-tar. Its structural formula is:



or

$$\begin{array}{ccc} CH & & CH \\ | & & | \\ C_6H_4 & — & C_6H_4 \end{array}$$

Phenanthrene is of interest on account of its relationship to morphine, codeine, and certain other opium alkaloids (p. 397).

CHAPTER XXXVI

SOME CONSTITUENTS OF ESSENTIAL OILS OF PLANTS

The volatile or essential oils of plants are entirely different, both in properties and in chemical composition, from the fixed or fatty vegetable oils (p. 274). They are, as a rule, light, mobile, highly odoriferous liquids, which are readily volatile, and can be distilled without decomposition. Most essential oils are optically active—an important point, since the specific rotation of an essential oil often provides a useful criterion of its purity.

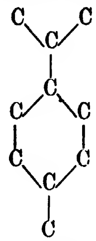
Chemically, the essential oils obtained from different plants differ widely in composition. Most of them are complex mixtures, although a few, such as Oleum Sinapis Volatile (p. 307) and Oleum Gaultheriæ (p. 366), consist of a single chemical compound in a state of comparative purity.

Many essential oils consist largely of hydrocarbons of a class known as the *terpenes*. These hydrocarbons are not themselves highly odorous, and such oils as contain them generally owe their characteristic odours to various compounds, such as alcohols, esters, aldehydes, ketones, and phenols, many of which are simple terpene derivatives. These odoriferous constituents are often present in the oil in comparatively small proportions, so that the terpene hydrocarbons act merely as diluents. The so-called "terpeneless" oils consist of essential oils from which the bulk of the terpene hydrocarbons have been separated by fractional distillation; they thus present the odoriferous and flavouring constituents of the oil in a highly concentrated form, and have the additional advantage of being less liable to decomposition on keeping.

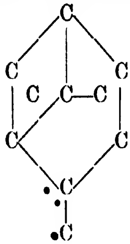
This chapter deals with the more important naturally occurring terpenes and related compounds. For descriptions of other constituents of essential oils see allyl isothiocyanate (p. 307), anethole (p. 348), thymol (p. 351), eugenol (p. 353), cinnamic aldehyde (p. 358), and methyl salicylate (p. 365).

The Terpenes

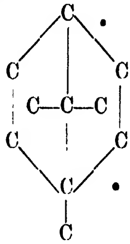
The simpler terpenes are related to cymene (p. 332) in that the carbon atoms are arranged within the molecule as follows:



Some of the more complex terpenes have what are known as "bridged ring" structures of such types as

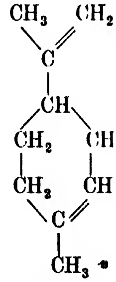


and



All the terpenes are isomeric, and have the molecular formula $C_{10}H_{16}$.

Limonene, $C_{10}H_{16}$, is a typical terpene, and has the following constitution :



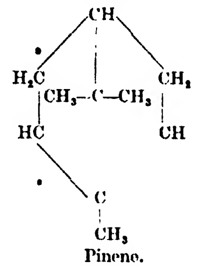
Limonene.

The molecule contains an asymmetric carbon atom, and the hydrocarbon exists in two optically active forms, both of which occur naturally. The *d*- form is the main constituent of Oleum Limonis, in which it occurs to the extent of about 90 per cent. The *l*- form is less commonly met with, but occurs to some extent in Oleum Menthæ Viridis (American and Russian). *dl*-Limonene, or *dipentene*, as it is usually called, is found in Oleum Cubebæ and in Russian oil of turpentine.

Limonene is a colourless liquid with a pleasant characteristic odour, and boils at 175°. Its molecule contains two double bonds, and, as might be expected, it combines directly with two molecular proportions of bromine to form a tetrabromide, $C_{10}H_{16}Br_4$.

When either *d*- or *l*-limonene is heated at about 250° in a sealed tube racemisation takes place, with formation of optically inactive dipentene.

Pinene, $C_{10}H_{16}$, is the commonest and most widely distributed of the terpene hydrocarbons, and has the structure



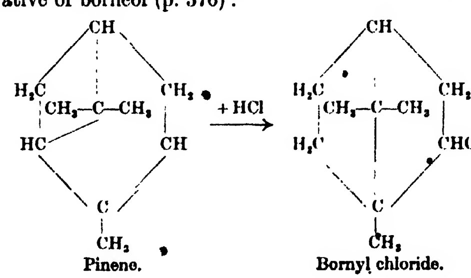
Pinene.

It contains two asymmetric carbon atoms, and exists in optically active forms.

Pinene is the main constituent of Oleum Terebinthinæ Rectificatum. The relative proportions of the *d*- and *l*- forms present vary widely with different samples of the oil: as a rule, the *d*- form preponderates in American samples and the *l*- form in French. Pinene also occurs in Oleum Eucalypti, Oleum Juniperi, Oleum Coriandri, Oleum Abietis, Oleum Rosmarini, and certain other essential oils.

Pinene is a colourless, mobile liquid, which boils at 155°, and has a characteristic odour resembling that of turpentine.

It is unsaturated, and combines with bromine to form a dibromide, $C_{10}H_{16}Br_2$. It also combines directly with one molecular proportion of hydrogen chloride; in this case the reaction does not consist of a simple addition of HCl to the double bond, but involves an interesting isomeric change, the product being *bornyl chloride*, a derivative of borneol (p. 376):



Pinene. Bornyl chloride.

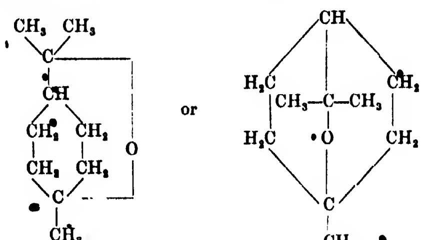
Bornyl chloride is a crystalline solid which closely resembles camphor in odour and other physical properties, and which for this reason is sometimes known as "artificial camphor".[1]

When shaken with sulphuric acid, pinene is converted into the isomeric hydrocarbon limonene. During the process racemisation takes place, so that the product from either *d*- or *l*-pinene is dipentene (*dl*-limonene). The official substance, **Terebenum,** *Terebene,* is prepared by shaking oil of turpentine with successive quantities of sulphuric acid until optically inactive. It consists of dipentene, mixed with smaller proportions of other hydrocarbons.

Amongst the other naturally occurring terpenes may be mentioned *camphene, sylvestrene,* and the *phellandrenes.* These are all isomeric with pinene and limonene.

Derivatives of the Terpenes

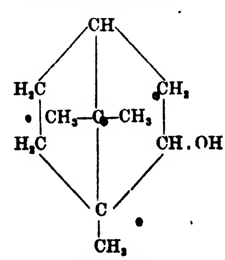
Cineol, $C_{10}H_{18}O$, has the structural formula



Cineol. or Cineol.

and is therefore a compound of the ether type (p. 228). It is the main constituent and active principle of Oleum Eucalypti and Oleum Cajuputi, which are required by the Pharmacopœia to contain, respectively, not less than 55 and 45 per cent of cineol.

Borneol, $C_{10}H_{18}O$, is a secondary alcohol of the formula



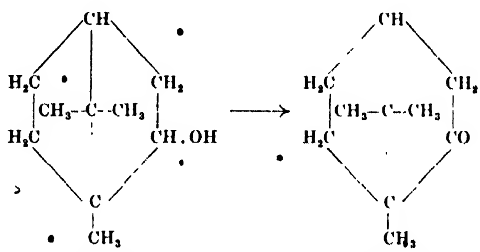
Borneol.

[1] Not to be confused with true synthetic camphor.

It occurs, both in the free state and as its acetate, in Oleum Abietis and Oleum Rosmarini.

Borneol is a crystalline solid with a characteristic odour recalling that of camphor, and is volatile in steam. Like other alcohols, it can react with acids to form esters. On treatment with phosphorus pentachloride it is converted into bornyl chloride, the —OH group being displaced by a chlorine atom.

Camphora, *Camphor,* $C_{10}H_{16}O$, is the ketone corresponding to the secondary alcohol borneol, from which it can be prepared by oxidation :

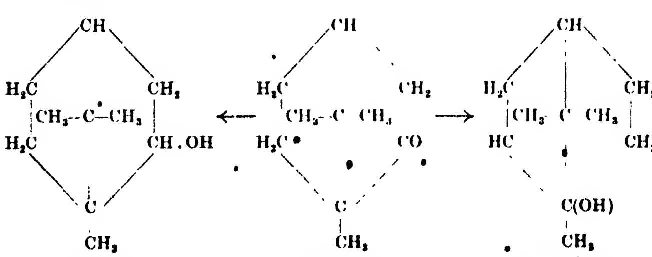


Borneol. Camphor.

Camphor occurs in Oleum Rosmarini, but it is generally obtained from the wood of the camphor tree, *Cinnamomum Camphora.*

Camphor is usually met with in colourless crystals, or as tough crystalline masses, having a penetrating and very characteristic odour. Melting-point about 175°. It readily sublimes on heating, and slowly volatilises even at ordinary temperatures.

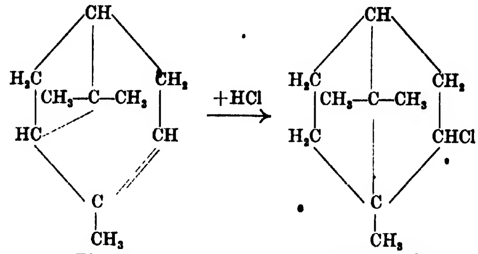
Being a ketone, it yields on reduction the corresponding alcohol, borneol, together with smaller quantities of isoborneol, the latter being produced as a result of isomeric change :



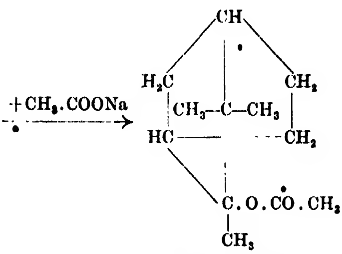
Borneol. Camphor. Isoborneol.

Camphor of the Pharmacopœia is the natural substance as obtained from *Cinnamomum Camphora,* but synthetic camphor is

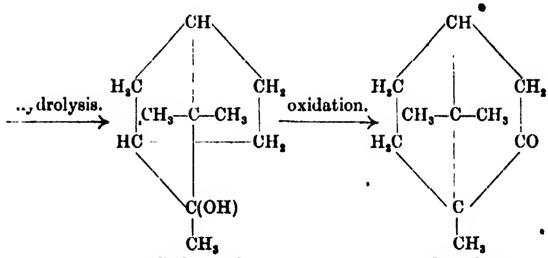
manufactured in considerable quantities from pinene by the following series of reactions :



Pinene. Bornyl chloride.



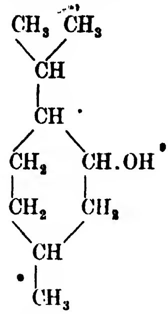
Isobornyl acetate.



Isoborneol. Camphor.

Synthetic camphor is optically inactive, whereas the official substance is dextro-rotatory, so the two can be easily distinguished.

Menthol, *Menthol*, $C_{10}H_{20}O$, is a secondary alcohol of the formula :

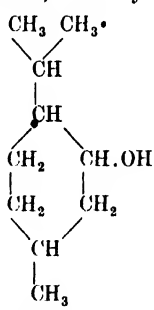


Menthol.

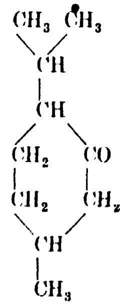
Menthol is usually obtained from the volatile oil of *Mentha arvensis*. It is the principal constituent of Oleum Menthæ Piperitæ, in which it occurs both in the free state and in the form of esters.

Menthol forms colourless crystals or crystalline masses, melting at 42°-43°, and having a characteristic odour and taste. It volatilises rapidly and completely at the temperature of the water-bath, and is lævo-rotatory.

On oxidation, menthol yields the corresponding ketone, *menthone*:



Menthol.



Menthone.

Menthone is a liquid, which also occurs in small quantities in Oleum Menthæ Piperitæ.

Open-chain Compounds related to the Terpenes

The compounds about to be described are open-chain compounds. Nevertheless, an inspection of their structural formulæ will show that they contain an arrangement of carbon atoms somewhat similar to that of limonene, the ring being broken at one point.

Citral, $\begin{matrix}CH_3\\CH_2\end{matrix}\!\!>\!C.CH_2.CH_2.CH_2.C(CH_3):CH.CHO$, is the chief

odoriferous constituent of Oleum Limonis, although it is only present to the extent of about 4 per cent. Oleum Graminis Citrati contains as much as 70-80 per cent of citral.

Citral is a colourless liquid, having the pleasant odour characteristic of oil of lemon. It boils at 224°-228°. It has the usual properties of an aldehyde ; thus, it forms an additive product with sodium bisulphite, and can be reduced to the alcohol, *geraniol*, and oxidised to the acid, *geranic acid* :

$$\begin{matrix} CH_3 \\ CH_2 \end{matrix}\!\!>\!C.CH_2.CH_2.CH_2.C(CH_3):CH.CH_2.OH.$$

Geraniol.

$$\begin{matrix} CH_3 \\ CH_2 \end{matrix}\!\!>\!C.CH_2.CH_2.CH_2.C(CH_3):CH.COOH.$$

Geranic acid.

Like other aldehydes, citral reacts with hydroxylamine to form an oxime, and it is upon this fact that the pharmacopœial method of estimation of citral in Oleum Limonis is based.

Citronellal, $\begin{matrix} CH_3 \\ CH_2 \end{matrix}\!\!>\!C.CH_2.CH_2.CH_2.CH(CH_3).CH_2.CHO$, occurs in Oleum Graminis Citrati and certain other essential oils. It is very similar to citral in structure and in properties.

Linalool, $\begin{matrix} CH_3 \\ CH_2 \end{matrix}\!\!>\!C.CH_2.CH_2.CH_2.\underset{\displaystyle OH}{\underset{|}{C}}(CH_3).CH:CH_2$, is a constituent of many essential oils. It contains an asymmetric carbon atom, and exists in optically isomeric forms. The *d*-form (sometimes known as *coriandrol*) forms about 90 per cent of Oleum Coriannri, and the *l*-form, which is more widely distributed, occurs in Oleum Lavandulæ, partly in the free state and partly as its acetate, and to a smaller extent in many other essential oils.

Linalool is an alcohol, and is isomeric with geraniol. Under the influence of various reagents it is readily transformed into geraniol by a process of isomeric change.

CHAPTER XXXVII

THE GLUCOSIDES

THE glucosides form an important class of naturally occurring vegetable substances. They are generally colourless, crystalline compounds which are easily hydrolysed by boiling dilute mineral acids, or by water in the presence of certain enzymes, with formation of a mixture of glucose and some other organic compound. Many naturally occurring compounds which are derived from sugars other than glucose are classed, for convenience, as glucosides. As an example may be mentioned the "glucoside" barbaloin, which occurs in aloes, and which is a derivative, not of glucose, but of a sugar known as *d*-arabinose.

The naturally occurring glucosides are all complex compounds; so before dealing with them we shall consider briefly a few simpler compounds of the glucoside type which have been made artificially in the laboratory.

The Methyl Glucosides.—The simplest glucosides known are two optical isomers, called respectively α- and β-methyl glucosides, both of which have the constitutional formula

$$CH_2(OH).CH(OH).CH.CH(OH).CH(OH).\mathbf{C}H.OCH_3.$$

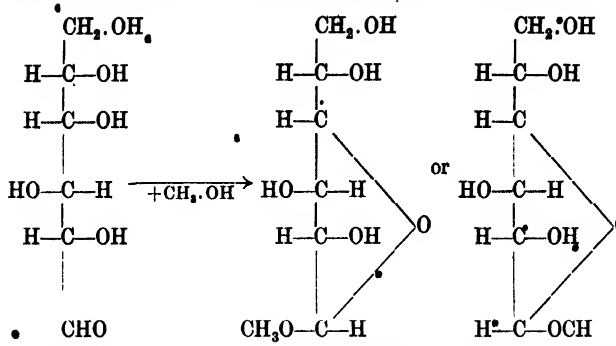
$$O$$

The carbon atom shown in heavy type is that which accounts for the existence of the two stereoisomers.

An equimolecular mixture of the methyl glucosides is formed by the action of hydrochloric acid, in the cold, on a solution of glucose in methyl alcohol. The reaction can be represented as shown at top of following page. The production of the glucosides thus involves a γ-lactone formation (p. 255). By the selective action of yeast on the mixture, and by fractional crystallisation, it has been found possible to separate it into its two components.

α- and β-methyl glucosides are both colourless crystalline compounds. They are hydrolysed by boiling dilute mineral acids, with formation of glucose and methyl alcohol in each case.

Other similar alkyl glucosides have been made synthetically.



Glucose. α-Methyl glucoside. β-Methyl glucoside.

THE NATURALLY OCCURRING GLUCOSIDES

The glucosides found in plants are probably similar in structure to the simpler synthetic alkyl glucosides. The group of atoms which takes the place of the alkyl radicle varies widely in the case of different natural glucosides, so that the product of hydrolysis other than glucose may be a phenol, an aromatic alcohol or aldehyde, a cyanogen compound, an anthraquinone derivative, or even an alkaloid. Many glucosides are of considerable pharmaceutical importance.

Salicinum, *Salicin,* $C_{13}H_{18}O_7$, is obtained from the bark of various species of *Salix* and of *Populus*.

Salicin is met with in colourless, glistening, crystalline plates, or as a white crystalline powder, having an exceedingly bitter taste. Melting point, 200°-201°. It is soluble 1 in 28 in water, less soluble in alcohol, and insoluble in ether.

On hydrolysis with water, in the presence of emulsin (p. 383), salicin is converted into glucose and saligenin :

$$C_{13}H_{18}O_7 + H_2O = C_6H_{12}O_6 + C_6H_4(OH).CH_2.OH.$$

Tests for Salicin.—(1) If a little concentrated sulphuric acid is added to salicin a deep red colour is developed in the cold.

(2) When warmed with potassium dichromate and dilute sulphuric acid salicin is oxidised with formation of salicylaldehyde, which can be recognised by its characteristic odour of meadow-sweet.

Amygdalin, $C_{20}H_{27}O_{11}N$, occurs to the extent of 2·5-4 per cent in the seeds of *Prunus Amygdalus*, var. *amara*.

It is a white crystalline powder, melting at 200°, and is readily soluble in water. When warmed with fairly concentrated sulphuric acid it is hydrolysed to glucose and bedzaldehyde cyanohydrin :

$$C_{20}H_{27}O_{11}N + 2H_2O = 2C_6H_{12}O_6 + C_6H_5.CH\left\langle\begin{array}{l}OH\\CN\end{array}\right.$$

Benzaldehyde cyanohydrin.

If boiling dilute hydrochloric acid is employed the reaction goes a stage further, the cyanohydrin being decomposed into benzaldehyde and hydrocyanic acid :

$$C_6H_5.CH\left\langle\begin{array}{l}OH\\CN\end{array}\right. \longrightarrow C_6H_5.CHO + HCN.$$

With hot concentrated hydrochloric acid the hydrolysis of amygdalin follows a different course, the final products being glucose, ammonium chloride, and *l*-mandelic acid :

$$C_{20}H_{27}O_{11}N + 4H_2O + HCl = 2C_6H_{12}O_6 + NH_4Cl + C_6H_5.CH\left\langle\begin{array}{l}OH\\COOH\end{array}\right.$$

Amygdalin is slowly hydrolysed to glucose, benzaldehyde, and hydrocyanic acid by cold water, in the presence of emulsin, a mixture of enzymes which occurs in bitter almonds. In the bitter almond seeds the amygdalin and emulsin occur in different cells. If, however, the seeds are crushed and macerated with water, and the mixture allowed to stand, the glucoside comes into contact with the enzyme and a strong odour of hydrocyanic acid is developed.

Sweet almonds (*P. Amygdalus*, var. *dulcis*) contain emulsin, but differ from bitter almonds in that they contain no amygdalin. They do not therefore develop any odour of hydrocyanic acid when macerated with water and allowed to stand.

Prulaurasin, $C_{14}H_{17}O_6N$, is the main active constituent of the fresh leaves of *Prunus Laurocerasus*.

Prulaurasin forms colourless crystals, with a bitter taste, which melt at 120°. Chemically it is very similar to amygdalin, and yields similar products on hydrolysis. Thus, when cherry laurel leaves are macerated with water, prunase, an enzyme present in the leaves, brings about the hydrolysis of the prulaurasin, with formation of glucose, benzaldehyde, and hydrocyanic acid (compare p. 300) :

$$C_{14}H_{17}O_6N + H_2O = C_6H_{12}O_6 + C_6H_5.CHO + HCN.$$

Arbutin, $C_{12}H_{16}O_7$, is a comparatively simple glucoside which occurs in the leaves of *Arctostaphylos Uva-ursi*. It crystallises in colourless needles containing half a molecular proportion of water of crystallisation, and melts at 168°. On hydrolysis, either with boiling dilute mineral acids or with water in the presence of emulsin, it yields glucose and hydroquinone (p. 353) :

$$C_{12}H_{16}O_7 + H_2O = C_6H_{12}O_6 + C_6H_4(OH)_2.$$

Sinigrin, $C_{10}H_{16}O_9NS_2K$, is a glucoside contained in black mustard

seeds (*Brassica sinapoides*) and in horse-radish root (*Cochlearia Armoracia*), accompanied by an enzyme called myrosin. When either of these drugs is macerated with water the enzyme is brought into contact with the glucoside, thus bringing about the hydrolysis of the latter to a mixture of glucose, allyl isothiocyanate, and potassium hydrogen sulphate :

$$C_{10}H_{16}O_9NS_2K + H_2O = C_6H_{12}O_6 + C_3H_5.NCS + KHSO_4.$$

Strophanthin is a glucoside, or mixture of glucosides, which occurs to the extent of 8-10 per cent in the seeds of *Strophanthus Kombé*. It is a white crystalline powder, readily soluble in water, and when boiled with dilute mineral acids it is hydrolysed with formation of a sugar and a compound called strophanthidin. The production of strophanthidin in this way forms the basis of a chemical method for the assay of strophanthus seeds.

When strophanthin is treated with 80 per cent sulphuric acid a deep green coloration is produced. This reaction is described in the Pharmacopœia as a test for the presence of the glucoside in strophanthus seeds.

Saponins.—These constitute a class of glucosides which occur in a large number of plants. They derive their general name from the fact that when shaken with water they dissolve, with the formation of a soap-like froth. They are protoplasmic poisons, being toxic when injected directly into the blood stream, but are much less so when taken by mouth. They are very toxic to certain cold-blooded animals, and many of them are strongly sternutatory.

Saponins are divided into two classes :

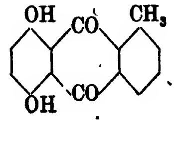
Acid Saponins, including polygalic acid (in senega), quillaic acid (in quillaia), and guaiacsaponic acid (in guaiacum).

Neutral Saponins, which are the more toxic, including senegin (in senega), quillaiasapotoxin (in quillaia), and guaiacsaponin (in guaiacum).

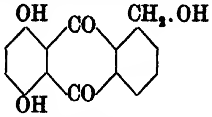
On hydrolysis, saponins yield various sugars, together with non-toxic, complex compounds known as sapogenins. Thus, for example, quillaic acid, $C_{19}H_{30}O_{10}$, yields galactose and another sugar and quillaiasapogenin.

Commercial "saponin" is a mixture of the saponins obtained from quillaia bark.

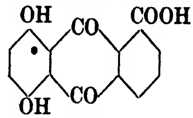
Anthraquinone Glucosides.—Many purgative drugs, such as senna, cascara, rhubarb, and aloes, contain glucosides which, on hydrolysis, yield derivatives of anthraquinone. Rhubarb, for example, contains a glucoside which on hydrolysis yields chrysophanic acid, a dihydroxymethylanthraquinone, which probably has the following structure :



Closely related to chrysophanic acid are aloe-emodin, which occurs in aloes, senna and rhubarb, and rhein, which occurs in senna and rhubarb. These compounds probably have the following structures :



Aloe-emodin.



Rhein.

Emodin, which occurs in cascara and rhubarb, is a hydroxy-derivative of chrysophanic acid of the formula $CH_3.C_{14}H_4O_2(OH)_3$.

These anthraquinone derivatives occur in purgative drugs both in the free state and as glucosides. The glucosides are, for the most part, devoid of purgative properties, with the notable exception of *barbaloin*, which is a glucoside derived from aloe-emodin and *d*-arabinose, and is the chief active constituent of aloes. The purgative properties of rhubarb appear to be due to a complex non-glucosidal resin, which on hydrolysis yields derivatives of anthraquinone, together with cinnamic and gallic acids. The active principles of senna and cascara are still unknown.

Gluco-resins.—Many drugs, such as jalap, orizaba jalap, turpeth, and scammony, contain considerable quantities of highly complex resins, which consist to a large extent of mixtures of glucosides. On hydrolysis these glucosidal resins yield a variety of products, including sugars and complex " resin acids ", such as convolvulinolic acid, ipurolic acid, and jalapinolic acid.

Estimation of Resin in Tinctura Jalapæ.—Tincture of Jalap is required to contain 1·5 grammes of jalap resin in 100 mils. The tincture may be assayed by the following process :

Concentrate 10 mils of the tincture in a small tared beaker on a water-bath until most of the alcohol has been removed. Add about 80 mils of water, slightly acidified with hydrochloric acid, and allow the precipitated resin to subside. Pour off the water, and wash by decantation with further quantities of water. Set aside in a water-oven to dry, and then weigh from time to time until the weight is constant. The resin obtained from 10 mils of tincture should weigh between 0·145 and 0·155 gramme.

Acidum Tannicum. *Tannic Acid.* *Syn.* Tannin.—This is a glucosidal substance obtained from galls. The powdered galls are exposed to a damp atmosphere for several days, when fermentation takes place. The product is mixed with water-saturated ether, and, after allowing to stand, the liquid is separated by filtration in presses through fine linen. The ethereal extract thus obtained is shaken with water, which dissolves out the tannic acid, leaving resins, colouring matter, and other impurities in the ether. The aqueous layer is separated and evaporated under diminished pressure, when the tannic acid remains as a pasty mass, which is dried on porous plates in a water-oven.

Tannic acid is a brownish powder, consisting of thin glistening scales. It has a characteristic odour and a strongly astringent taste, and is freely soluble in water, alcohol (90 per cent), and glycerin, but very sparingly in dry ether. The aqueous solution has an acid reaction.

Many mineral acids and salts precipitate tannic acid from its aqueous solution. Its aqueous solution precipitates solutions of isinglass, albumen, alkaloids, and tartarated antimony, and gives with ferric chloride a deep bluish-black colour.

The pharmacopœial formula of tannic acid is $C_{14}H_{10}O_9$, but this is only an approximate empirical formula. In reality tannic acid is a complex condensation product of glucose and gallic acid, and is probably pentadigalloyl glucose (the digalloyl group being $C_6H_2(OH)_3.CO.O.C_6H_2(OH)_2.CO—$):

$$
\begin{array}{l}
CH_2.O.CO.C_6H_2(OH)_2.O.CO.C_6H_2(OH)_3 \\
| \\
CH.O.CO.C_6H_2(OH)_2.O.CO.C_6H_2(OH)_3 \\
| \\
CH.O.CO.C_6H_2(OH)_2.O.CO.C_6H_2(OH)_3 \\
| \\
CH.O.CO.C_6H_2(OH)_2.O.CO.C_6H_2(OH)_3 \\
| \\
CH.O.CO.C_6H_2(OH)_2.O.CO.C_6H_2(OH)_3 \\
| \\
CHO.
\end{array}
$$

Pentadigalloyl glucose.

Pentadigalloyl glucose would have the molecular formula $C_{76}H_{52}O_{46}$, and this is in fairly close agreement with the empirical formula $C_{14}H_{10}O_9$. When tannic acid is boiled with dilute sulphuric acid it is hydrolysed with formation of glucose and gallic acid:

$$C_{76}H_{52}O_{46} + 10H_2O = C_6H_{12}O_6 + 10C_6H_2(OH)_3.COOH.$$

Tannic acid is the most important of a class of substances known as tannins, which are all derivatives of polyhydroxy-aromatic acids. They owe their generic name to the fact that they are the active constituents of materials, such as oak bark, which are used in tanning skins. Tannins occur in a very large number of vegetable drugs, and are present in tinctures, etc., prepared from them. Many of these preparations, on keeping, deposit insoluble magmas, consisting of complex oxidation products of the tannins, known as phlobaphenes.

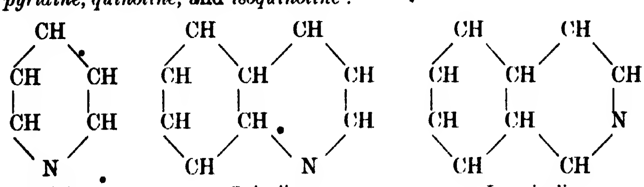
Commercial varieties of tannic acid, as used in dyeing and in the manufacture of inks, frequently contain free gallic acid, and are not suitable for medicinal use.

CHAPTER XXXVIII

THE ALKALOIDS AND RELATED COMPOUNDS

THE term "vegetable alkaloid" is not easy to define, but in its widest sense it may be said to include all basic nitrogenous organic compounds which occur in plants. Many of these compounds have marked physiological properties, and for this reason the alkaloids form one of the most important groups of organic medicinal chemicals. Many compounds have been prepared in the laboratory which have never been found in plants, but which closely resemble one or other of the naturally occurring alkaloids in constitution and in physiological action. Such compounds are often known as "synthetic alkaloids". Over two hundred well-defined vegetable alkaloids are known at the present time, and this number is being continually added to as different plant products are investigated; it is, therefore, only possible to describe here a few of the more important alkaloids employed in medicine.

Most alkaloids are highly complex compounds. Many of them are derivatives of one or other of three tertiary aromatic bases—*pyridine*, *quinoline*, and *isoquinoline*:



Pyridine. Quinoline. Isoquinoline.

Pyridine is closely related to benzene, from which it differs only in the fact that a nitrogen atom takes the place of one of the $>$CH groups of the ring; the problem of its constitution is similar to that of benzene in that the exact dispositions of the fourth valency bonds of the carbon atoms, and of the third valency bond of the nitrogen atom, are unknown. Quinoline and isoquinoline are, in a similar way, related to naphthalene.

All three compounds occur, in small quantities, in coal-tar. Pyridine is an evil-smelling liquid, and is generally obtained from

the "bone oil" produced by the destructive distillation of bones. Quinoline is an oily liquid, having an odour which is characteristic, but not so disagreeable as that of pyridine. Isoquinoline is a crystalline solid of low melting-point.

Pyridine, quinoline, and isoquinoline are more or less similar in chemical properties to the tertiary aliphatic amines. They are fairly strong monacid bases, their aqueous solutions being alkaline to litmus, and they combine with acids to form stable crystalline salts. Being tertiary bases, they do not react with nitrous acid. Like the corresponding aromatic hydrocarbons, they are very stable compounds, and pyridine in particular is not readily attacked by sulphuric or nitric acids, halogens, or oxidising agents.

The close relationship of pyridine, quinoline, and isoquinoline to certain alkaloids is shown by the fact that, when the molecule of an alkaloid is broken up by oxidation, distillation over zinc dust, or in some other way, one or more of these bases, or their simpler derivatives, are not infrequently to be found amongst the disintegration products. It must not be thought, however, that all alkaloids are derivatives of pyridine, quinoline, or isoquinoline; in fact, many, such as cocaine, hyoscyamine, and caffeine, are not even distantly related to them.

General Tests for Alkaloids.—(1) All the official alkaloids are white or colourless crystalline solids, which char on heating in a dry test-tube, emitting an odour resembling that of singed hair. They are all insoluble or sparingly soluble in water, but dissolve readily in dilute hydrochloric acid with formation of hydrochlorides. From such solutions they are precipitated on the addition of excess of sodium carbonate.

(2) The salts of the official alkaloids are crystalline compounds, and are, generally, readily soluble in water. From their aqueous solutions the addition of excess of sodium carbonate precipitates the free alkaloids.

(3) *Mayer's reagent*, potassio-mercuric iodide, made by adding excess of potassium iodide solution to a solution of mercuric chloride, gives, with solutions of alkaloids in the minimum quantity of dilute hydrochloric acid, a white or pale yellow precipitate. Caffeine and theobromine do not give this precipitate.

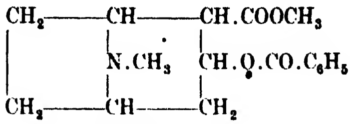
(4) *Dragendorff's reagent*, potassio-bismuth iodide, made by adding excess of potassium iodide solution to a solution of bismuth nitrate, gives with solutions of alkaloids in dilute mineral acid an orange or orange-red precipitate.

COCAINE, $C_{17}H_{21}NO_4$

Cocaine is the most important of a number of alkaloids which occur in the leaves of *Erythroxylum Coca* and its varieties. As a rule, the leaves contain something less than 1 per cent of total alkaloids.

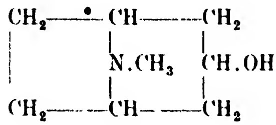
Cocaine is a monacid tertiary base, and forms crystalline salts

with one equivalent of an acid. It has the following comparatively simple structure :



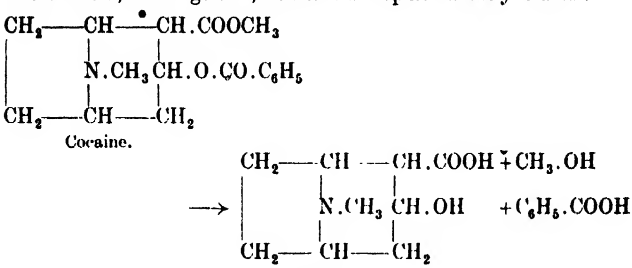
Cocaine.

It is a derivative of the base tropine, from which many other alkaloids are derived :



Tropine.

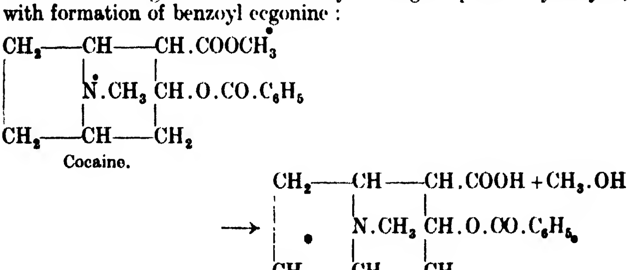
Boiling dilute acids or alkalies hydrolyse cocaine to methyl alcohol, benzoic acid, and ecgonine, which is a tropine carboxylic acid :



Cocaine.

Ecgonine.

But with boiling water cocaine only undergoes partial hydrolysis, with formation of benzoyl ecgonine :



Cocaine.

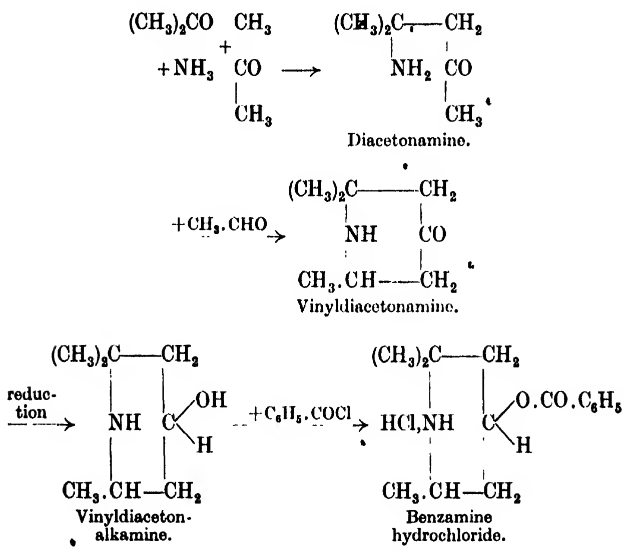
Benzoyl ecgonine.

Tests for Cocaine.—(1) Warm with concentrated sulphuric acid. Charring takes place, a pleasant odour of methyl benzoate (somewhat similar to that of oil of wintergreen) is evolved, and a sublimate of benzoic acid forms on the sides of the tube.

(2) Moisten with concentrated nitric acid, evaporate just to dryness, and add about .1 mil of alcoholic potash. A pleasant odour is evolved, recalling peppermint.

Benzamine, β-eucaine, $C_{15}H_{21}NO_2$, is an important synthetic alkaloid, which closely resembles cocaine both in structure and in physiological action.[1]

It is prepared by the following interesting synthetic process. 2 molecules of acetone are condensed with 1 of ammonia, and the product is allowed to react with acetaldehyde to form a ketone, vinyldiacetonamine. This on reduction gives a secondary alcohol, vinyldiaceton-alkamine, which when treated with benzoyl chloride is converted into the hydrochloride of benzamine :



Benzamine is a crystalline compound, and has the usual properties of a strong monacid secondary base. It is the most important of a group of synthetic alkaloids which have, to a considerable extent, replaced cocaine as a local anæsthetic.

[1] This and other alkaloids of lesser importance to the student are only described in general terms, even though they or their salts may be official. A complete list of official alkaloids and alkaloidal salts is given on p. 404.

COCAINA

Cocaine

Preparation.—(1) Powdered coca leaves are moistened with sodium hydroxide solution and percolated with petroleum spirit. From the organic solvent the alkaloid is extracted as its sulphate by means of dilute sulphuric acid. The acid solution is then made alkaline with sodium hydroxide, and the precipitated cocaine is purified by crystallisation from ether.

(2) Considerable quantities of cocaine are obtained from crude "cake alkaloid" extracted from coca leaves, shortly after collection, in the countries where they are grown. The mixture of crude alkaloids (cocaine, cinnamyl-cocaine, and iso-tropyl-cocaine) is submitted to hydrolysis, and the ecgonine thus produced is, after purification, converted into cocaine by esterification with methyl alcohol and sulphuric acid, and subsequent treatment of the methyl ecgonine with benzoyl chloride.

Properties.—Colourless, monoclinic prisms, melting at 98°, and having a slightly bitter taste, followed by tingling and numbness. Soluble about 1-1300 in water and 1-10 in alcohol (90 per cent).

Tests for Impurities.—The product obtained by dissolving in dilute hydrochloric acid and evaporating to dryness on a water-bath should be free from the impurities described under Cocainæ Hydrochloridum.

COCAINÆ HYDROCHLORIDUM

Cocaine Hydrochloride

Preparation.—This is the product actually obtained as the result of the benzoylation of methyl ecgonine. It may be prepared from cocaine by dissolving in dilute hydrochloric acid, evaporating to dryness, and recrystallising the residue from a mixture of alcohol and ether.

Properties.—Colourless prisms or a crystalline powder, soluble 1-0·5 in water and 1-3 in alcohol (90 per cent). Melting-point, 182°-186°. It should be stored in well-stoppered bottles of amber-coloured glass, as it tends to decompose under influence of moisture and light.

Tests for Impurities. *Moisture* (*Limit of*).—It should lose not more than 1 per cent of its weight when dried at 100°.

Metallic Compounds.—On ignition, it should leave no appreciable ash.

Readily Carbonisable Organic Compounds and certain other Alkaloids.—0·05 gramme should dissolve in 1 mil of cold concentrated sulphuric or nitric acid without coloration.

Cinnamyl-cocaine and certain other Coca Alkaloids.—3 drops of N/10 potassium permanganate added to a solution of 0·1 gramme of the salt in a mixture of 5 mils of water and 3 drops of dilute sulphuric

acid gives a violet colour, which, if dust is carefully excluded, should not fade in half an hour.

Amorphous Alkaloids (*Limit of*).—When 0·25 mil of Solution of Ammonia is mixed with a solution of 0·1 gramme of the salt in 100 mils of water contained in a glass beaker and the mixture set aside for fifteen minutes, the sides of the beaker being occasionally but not too vigorously rubbed with a glass rod, the cocaine separates as a crystalline precipitate, and the supernatant liquid should remain perfectly clear.

ATROPINE, $C_{17}H_{23}NO_3$

Atropine can be extracted from the root or leaves of *Atropa Belladonna*, but commercially it is generally obtained from *Hyoscyamus muticus*.

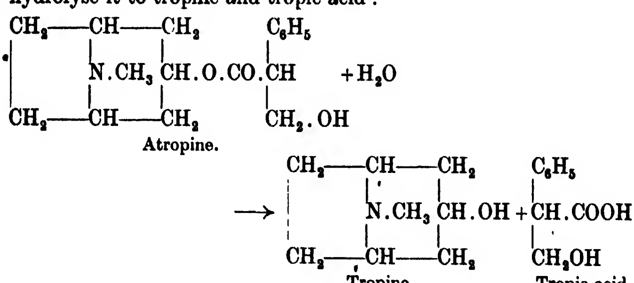
Atropine is met with in colourless crystals or as a crystalline powder, sparingly soluble in water, readily in alcohol, ether, and chloroform. When pure it melts at 114·5°-115·5°, but the commercial alkaloid often contains a small quantity of hyoscyamine, which lowers the melting-point. Atropine is optically inactive.

Atropine is a derivative of tropine, being, in fact, the tropyl ester of tropic acid :

$$C_6H_5.CH\begin{cases}CH_2OH\\COOH.\end{cases}$$

Tropic acid.

Like cocaine, atropine is a monacid tertiary base, and forms salts with one equivalent of an acid. Boiling dilute acids or alkalies hydrolyse it to tropine and tropic acid :

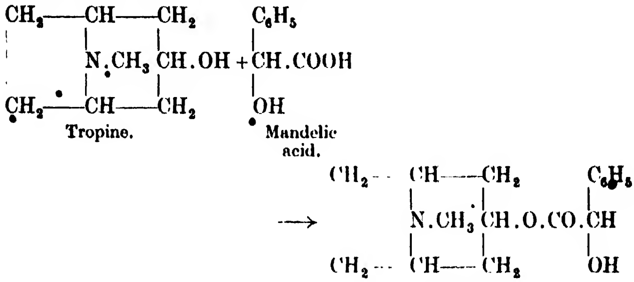


Atropine. Tropine. Tropic acid.

Hyoscyamine, $C_{17}H_{23}NO_3$, is the *l*-form of the alkaloid of which atropine is the racemic form. The two alkaloids are therefore identical in chemical properties, though they differ slightly in such physical properties as melting-point, crystalline form, and solubility. Hyoscyamine occurs in *Atropa Belladonna*, *Hyoscyamus niger*, *Hyoscyamus muticus*, and other Solanaceous plants. The alkaloid extracted from any of these sources is a mixture of atropine and hyoscyamine in varying proportions, together with smaller quantities

of hyoscine and other alkaloids. In most cases atropine is not actually present in the plant, but is formed by racemisation of some of the hyoscyamine during the process of extraction.

Homatropine, $C_{16}H_{21}NO_3$, is a well-known synthetic alkaloid which is very closely related to atropine. It is prepared by the interaction of tropine and mandelic acid :



Tropine. Mandelic acid. Homatropine.

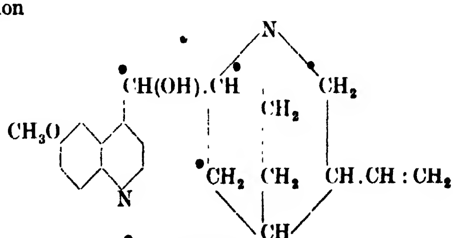
Homatropine was introduced into ophthalmic practice as an alternative to atropine, to which it is very similar in physiological action.

Quinine, $C_{20}H_{24}N_2O_2$

This important alkaloid is obtained from the bark of various species of *Cinchona*. The amounts of total alkaloid contained in different cinchona barks vary considerably, the average being about 6-10 per cent. Quinine usually makes up about one-quarter of the total alkaloid, the remainder consisting of quinidine, cinchonine, cinchonidine, and a number of alkaloids of lesser importance. All the alkaloids are present in the bark in combination with various complex organic acids, such as quinic and cinchotannic acids.

Quinine crystallises in colourless needles containing 3 molecules of water of crystallisation. It is sparingly soluble in water, but dissolves readily in organic solvents. It has an intensely bitter taste, and is lævorotatory.

Quinine is a derivative of quinoline, and probably has the constitution

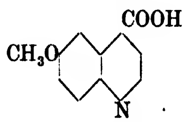


Quinine.

It is a di-acid tertiary base, and forms salts with two equivalents of an acid.

It is noteworthy that the monacid salts of quinine are generally much less soluble in water than the di-acid salts. Thus the mono-hydrochloride (Quininæ Hydrochloridum) is soluble 1-36 and the di-hydrochloride (Quininæ Hydrochloridum Acidum) more than 1-1. The mono-sulphate (Quininæ Sulphas) is only sparingly soluble (1-800) in water, an unusual property for an alkaloidal salt; it dissolves freely in dilute mineral acid, with formation of di-acid salts.

On oxidation with chromic acid quinine is decomposed with formation of quininic acid, a derivative of quinoline:



Quininic acid.

This fact shows clearly the close relationship of quinine to quinoline.

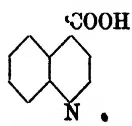
Tests for Quinine.—(1) A dilute solution of quinine or a quinine salt in dilute sulphuric acid shows a characteristic blue fluorescence.

(2) Dissolve a small quantity of quinine in a few drops of concentrated sulphuric acid in a porcelain dish. The solution is colourless, but becomes green on addition of a crystal of potassium dichromate.

(3) To about 10 mils of an approximately 1-1000 solution of a quinine salt add about 0·5 mil of bromine water, shake well, and add 3 drops of Solution of Ammonia, when a bright green coloration is produced. This is a very reliable test, provided that the reagents are added in approximately correct proportions.

Quinidine, $C_{20}H_{24}N_2O_2$, is similar to quinine in chemical properties, but is dextrorotatory. It appears to be a stereoisomer of quinine.

Cinchonine, $C_{19}H_{22}N_2O$, is identical in structure with quinine, except that it does not contain the CH_3O— group. Like quinine, it is a di-acid tertiary base. When oxidised it yields, not quininic, but cinchoninic acid:



Cinchoninic acid.

Cinchonidine, $C_{19}H_{22}N_2O$, is probably a stereoisomer of cinchonine.

QUININÆ SULPHAS

Quinine Sulphate

Preparation.—Most of the "quinine" of commerce is obtained from the bark of *Cinchona Ledgeriana*, which is largely grown in Java and South America, but considerable quantities of bark are now being imported from India.[1]

The powdered bark is intimately mixed with sodium hydroxide solution and slaked lime. The liberated alkaloids are extracted with hot petroleum, which is separated and shaken with the requisite quantity of hot, very dilute sulphuric acid, when the alkaloids pass into the aqueous layer as normal sulphates. The aqueous liquid is separated and cooled, when the sparingly soluble quinine sulphate crystallises out. The product is redissolved in boiling water, decolorised with animal charcoal, and recrystallised.

Properties.—Small, light, colourless, silky needles having an intensely bitter taste. Soluble 1-800 in water and 1-65 in alcohol (90 per cent), the aqueous solution having a faint blue fluorescence. Freely soluble in dilute mineral acids. On exposure to air the crystals effloresce, the water of crystallisation being reduced from 7½ molecules to 2 molecules.

Tests for Impurities. *Metallic Compounds.*—On ignition, it should leave no appreciable ash.

Ammonium Sulphate and Inorganic Salts.—1 gramme should dissolve completely in 7 mils of a mixture of 2 volumes of chloroform and 1 volume of absolute alcohol.

Other Cinchona Alkaloids (*Limit of*).—This test depends upon the facts that the sulphates of other Cinchona alkaloids are more soluble in water than is quinine sulphate, and that free quinine is easily soluble in excess of ammonium hydroxide, whereas other Cinchona alkaloids are not. Digest 2 grammes of the salt (weighed after drying at 50°) with 20 mils of water in a stoppered test tube at 60°-65° for half an hour, with frequent shaking. Cool to 15°, keep at this temperature for half an hour, stirring occasionally, press the crystals, and filter the expressed liquid. Transfer 5 mils of this filtrate to a dry test tube, bring to a temperature of 15°, and gradually add Solution of Ammonia, also at a temperature of 15°, from a burette. The precipitate produced should redissolve on rotating the tube, when not more than 6 mils of the Solution of Ammonia have been added.

QUININÆ HYDROCHLORIDUM

Quinine Hydrochloride

Preparation.—(1) Quinine, freshly precipitated from an acid solution of its sulphate by means of slight excess of sodium

[1] Quinine issued from Government factories in India is coloured pink, in order to distinguish it from other commercial varieties.

carbonate or ammonia, is dissolved in sufficient dilute hydrochloric acid to produce a neutral solution, which is set aside to crystallise.

(2) It may also be obtained by double decomposition between barium chloride solution and quinine sulphate.

Properties.—Colourless, silky, slightly efflorescent crystals. Soluble 1·36 in water and 1·2 in alcohol (90 per cent), forming neutral or faintly alkaline solutions.

Tests for Impurities. *Metallic Compounds.*—On ignition, it should leave no appreciable ash.

Ammonium Sulphate and Inorganic Salts.—Test as under Quininæ Sulphas.

Barium.—The aqueous solution should yield no turbidity on the addition of dilute sulphuric acid.

Sulphate.—The aqueous solution should yield no turbidity on the addition of barium chloride.

Readily Carbonisable Organic Compounds and certain other Alkaloids.—It should dissolve without coloration in cold, concentrated sulphuric or nitric acid.

Other Cinchona Alkaloids (Limit of).—The Pharmacopœia says: "When 2 grammes are dissolved in a warm mortar in 20 millilitres of water at 60°, 1 gramme of powdered non-effloresced sodium sulphate added, the mixture triturated, cooled, allowed to stand at exactly 15° for half an hour with occasional stirring, the crystals of quinine sulphate pressed, and the expressed liquid filtered, 5 millilitres of this filtrate, transferred to a dry test tube and brought to a temperature of 15°, yield, on the gradual addition of 6 millilitres of Solution of Ammonia, also at a temperature of 15°, a precipitate which redissolves on rotating the tube."

The B.P.C. suggests the following more accurate process: Mix 2 grammes of the salt with 10 mils of water in a separator, add a slight excess of ammonium hydroxide, extract the alkaloid by shaking with ether several times, evaporate the ethereal solution, dissolve the residual alkaloid in alcohol, and exactly neutralise it with dilute sulphuric acid. Evaporate the neutral solution to dryness, and test the residue of quinine sulphate as described under Quininæ Sulphas.

Quantitative Test.—It should lose not more than 9·1 per cent of its weight when dried at 100° (equivalent to 2 molecules of water of crystallisation).

Quininæ Hydrochloridum Acidum. *Acid Quinine Hydrochloride.*—This may be prepared by dissolving quinine or quinine hydrochloride in excess of dilute hydrochloric acid and crystallising, or by double decomposition between solutions of barium chloride and quinine acid sulphate.

Properties.—A white crystalline or amorphous powder, soluble 2·1·5 in water, forming an acid solution; soluble 1·5 in alcohol (90 per cent).

Tests for Impurities.—Dissolve 2 grammes in 15 mils of water,

neutralise the solution with N/1 sodium hydroxide, mix with 1 gramme of powdered, non-effloresced sodium sulphate, and proceed as described in the pharmacopœial test under Quininæ Hydrochloridum (Limit of other Cinchona Alkaloids), or the alternative method there described may be employed.

On ignition, Quininæ Hydrochloridum Acidum should leave no appreciable ash. When dried at 100° it should lose not more than 3 per cent of its weight (Limit of Moisture).

Quantitative Test.—1 gramme dissolved in 20 mils of water should require for neutralisation not more than 5·0 mils of N/1 sodium hydroxide, using phenolphthalein as indicator.

MORPHINE, $C_{17}H_{19}NO_3$

Morphine was the first alkaloid to be discovered, and is the chief alkaloidal constituent and active medicinal principle of opium, good average samples of which contain about 10 per cent of morphine. Some twenty other alkaloids have been isolated from opium, and of these the more important are narcotine, papaverine, thebaine, narceine, and codeine. Most of the morphine in opium is present as sulphate or in combination with a crystalline aliphatic acid, known as meconic acid, of the formula $C_5H_2O_3(COOH)_2,3H_2O$. Traces of meconic acid can be easily detected by delicate colour reactions—a fact of considerable importance in toxicology, since the presence of meconic acid is a very strong indication of the presence of opium, in contradistinction to morphine *per se*.

Morphine is a colourless crystalline compound, very sparingly soluble in water, and having an intensely bitter taste. Chemically, it is a very complex compound, and its structure is not definitely known. It is probably a derivative of phenanthrene.

Morphine is a monacid tertiary base, forming salts with one equivalent of an acid. It differs from most of the other common alkaloids in that it has phenolic as well as basic properties. If, for instance, sodium, potassium, or calcium hydroxide is added to an aqueous solution of a morphine salt, the precipitate of the free alkaloid at first produced redissolves in excess of the precipitant, owing to the formation of a soluble metallic derivative. With ammonium hydroxide, however, the precipitate is only with difficulty soluble in excess. In forming metallic salts, morphine reacts with one equivalent of an alkali, showing that its molecule contains one phenolic —OH group. Another —OH group, which is probably alcoholic, is also present.

When morphine is distilled over zinc dust it is decomposed with formation of a number of simpler compounds, among which are pyridine and quinoline.

Tests for Morphine.—(1) Its solubility in aqueous sodium hydroxide serves to distinguish morphine from other common alkaloids.

(2) Morphine liberates iodine from iodic acid. When a dilute,

acid solution of a morphine salt is added to a solution of potassium iodate containing starch mucilage a deep blue coloration is at once produced.

(3) A solution of a morphine salt gives with ferric chloride a greenish-blue colour. If to this liquid potassium ferricyanide be added a deep blue precipitate of Prussian blue is produced.

(4) Dissolve about 0·1 gramme of morphine or a morphine salt in about 2 mils of concentrated sulphuric acid, heat the solution on a water-bath for fifteen minutes, cool, and add a few drops of dilute nitric acid. A deep violet colour is produced, changing rapidly to blood-red. This is a very delicate test.

Codeine, $C_{18}H_{21}NO_3$, is an alkaloid which occurs in opium. It is derived theoretically from morphine by the displacement of the hydrogen atom of the phenolic —OH group by the methyl group, —CH_3, and it can, in fact, be prepared from morphine by the action of methyl iodide in the presence of potassium hydroxide.

Codeine forms colourless crystals, sparingly soluble in water, the aqueous solution having a bitter taste and an alkaline reaction. Like morphine, it is a monacid tertiary base, and dissolves freely in dilute mineral acids with formation of salts ; but, as its molecule does not contain a free phenolic —OH group, it does not dissolve in aqueous alkalies.

Apomorphine, $C_{17}H_{17}NO_2$, does not occur naturally, but can be produced from morphine by the removal of a molecule of water. The hydrochloride is prepared for medicinal purposes by heating morphine with hydrochloric acid in sealed tubes.

Diamorphine, $C_{21}H_{23}NO_5$, sometimes known as "heroin", is the diacetyl derivative of morphine, the hydrogen atoms of both —OH groups having been displaced by acetyl groups ($CH_3.CO$—). Diamorphine is prepared from morphine by the action of acetic anhydride (p. 250).

MORPHINÆ HYDROCHLORIDUM

Morphine Hydrochloride

Preparation.—Morphine is usually extracted from Smyrna opium, which contains from 12-20 per cent, according to variety. The powdered opium is levigated with calcium chloride solution, whereupon double decomposition takes place with precipitation of calcium meconate and sulphate, all the alkaloids present being converted into soluble hydrochlorides. Hot water is added and the liquid filtered, sodium sulphite being added to the filtrate to prevent oxidation of the morphine. The liquid is next concentrated by evaporation, and sodium acetate is added to precipitate narcotine and other alkaloids, which are filtered off. The morphine is precipitated by the addition of calcium hydroxide and ammonium chloride, which interact with liberation of free ammonia, a little alcohol being previously added to induce the crystallisation of the

morphine. The codeine remains in the filtrate. The morphine is freed from any traces of remaining alkaloids by washing with benzene, and is then converted into the hydrochloride by dissolving in sufficient hydrochloric acid to produce a neutral solution, and crystallising.

Properties.—Colourless needles or a white, microcrystalline powder. Soluble 1-25 in water and 1-50 in alcohol (90 per cent), forming neutral solutions.

Tests for Impurities. *Metallic Compounds.*—On ignition, the ash, if any, should be too small to be weighable.

Narcotine and certain other Alkaloids.—The precipitate of free alkaloid produced on the addition of ammonium hydroxide to the aqueous solution should yield, after filtering and drying, not more than a trace to benzene.

Narcotine, Narceine, and Thebaine.—It should dissolve in cold, concentrated sulphuric acid with not more than a faint and transient pink colour.

Apomorphine.—One drop of potassium carbonate solution added to 5 mils of a 1-30 aqueous solution should yield a pure white precipitate. The precipitate should remain white on exposure to air, and should impart no reddish colour to chloroform when shaken with it.

Quantitative Test.—When dried at 100° it should lose about 14 per cent of its weight (equivalent to 3 molecules of water of crystallisation).

Quantitative Estimation.—Weigh 2 grammes of the crystalline salt, dissolve in 50 mils of warm, morphinated water (p. 414), add a slight excess of ammonium hydroxide, cool, filter off the precipitate, wash it with cold, morphinated water, and dry at 115°:

$$C_{17}H_{19}NO_3 \equiv C_{17}H_{19}NO_3,HCl,3H_2O,$$
$$285 \text{ grammes} = 375 \cdot 5 \text{ grammes.}$$

The Pharmacopœia requires that the precipitate from 2 grammes shall weigh from 1·50 to 1·52 grammes, corresponding to 75 to 76 per cent of anhydrous morphine.

Morphinæ Acetas. *Morphine Acetate.*—This is prepared by suspending freshly precipitated morphine in water, neutralising with acetic acid, evaporating on a water-bath until the product solidifies on cooling, and then drying the salt at a gentle heat.

Properties.—A white crystalline or amorphous powder. Almost entirely soluble 1-2·5 in water; soluble 1-100 in alcohol (90 per cent). On exposure to air it slowly loses acetic acid, becoming basic, and may become brownish in colour. On this account the aqueous solutions are usually slightly turbid.

Test for Impurities.—On ignition, it should leave no appreciable ash (absence of metallic compounds).

Quantitative Estimation.—Dissolve 2 grammes in 5 mils of warm, morphinated water, with the addition of about 0·1 mil of acetic

acid, and estimate the morphine gravimetrically, as described under Morphinæ Hydrochloridum :

$$C_{17}H_{19}NO_3 \equiv C_{17}H_{19}NO_3,C_2H_4O_2,3H_2O,$$
$$285 \text{ grammes} \equiv 399 \text{ grammes}.$$

The Pharmacopœia requires that the precipitate from 2 grammes of the salt shall weigh from 1·41 to 1·44 grammes, corresponding to 70·5 to 72·0 per cent of anhydrous morphine.

Morphinæ Tartras. *Morphine Tartrate.*—This is prepared by suspending morphine in water, neutralising with tartaric acid, and evaporating to crystallisation at a gentle heat.

Properties.—Minute, colourless needles, sometimes conglutinated. Efflorescent at 20°. Soluble 1-11 in water, forming a clear, neutral solution ; sparingly soluble in alcohol (90 per cent).

Test for Impurities.—On ignition, it should leave no appreciable ash (absence of metallic compounds).

Quantitative Estimation.—Dissolve 2 grammes in 20 mils of warm, morphinated water, and estimate the morphine gravimetrically, as described under Morphinæ Hydrochloridum :

$$2C_{17}H_{19}NO_3 \equiv (C_{17}H_{19}NO_3)_2,C_4H_6O_6,3H_2O,$$
$$2 \times 285 \text{ grammes} \equiv 774 \text{ grammes}.$$

The Pharmacopœia requires that the precipitate from 2 grammes shall weigh from 1·46 to 1·49 grammes, corresponding to 73 to 74·5 per cent of anhydrous morphine.

Solutions of Morphine Salts.—The above morphine salts are included in three official liquors, all of which are 1 per cent solutions. In the cases of the hydrochloride and the acetate, a little of the corresponding acid is added to the solution to compensate for the instability of the salts. In the case of the more stable tartrate this is unnecessary. The stability of the tartrate accounts for its use in the official hypodermic injection.

STRYCHNINE, $C_{21}H_{22}N_2O_2$

Strychnine occurs, together with the closely related alkaloid brucine, in the seeds of *Strychnos Nux-vomica* and other species of *Strychnos*. Nux vomica seeds usually contain about 3 per cent of total alkaloids, of which about one-half is strychnine.

Strychnine is a very complex alkaloid, and its constitution is not known with certainty. It is probably a derivative of quinoline.

Although the molecule contains two nitrogen atoms, strychnine is a monacid tertiary base, and combines with only one equivalent of acids to form salts.

Test for Strychnine.—Dissolve a fragment in a few drops of concentrated sulphuric acid in a porcelain dish, and add a little powdered potassium dichromate to the solution. An intense violet

colour is produced, changing on standing first to red and then to yellow. This test is sufficiently delicate to serve for the detection of less than a milligram of strychnine.

Brucine, $C_{23}H_{26}N_2O_4$, is very closely related to strychnine, from which it is probably theoretically derived by the displacement of two hydrogen atoms by methoxy groups ($CH_3.O$—). Therapeutically, brucine is much less active than strychnine, being only about one-tenth as toxic, and for this reason the pharmacopœial assay of Nux Vomica is an estimation, not of total alkaloids, but of strychnine only.

Brucine, like strychnine, is a monacid tertiary base. A solution of a brucine salt gives, with a trace of nitric acid, a deep red coloration. This test serves to distinguish brucine from strychnine, and is used to detect traces of brucine present as impurity in strychnine; it can also be employed as a delicate test for nitrate, as, for example, in water analysis (see p. 2).

STRYCHNINA

Strychnine

Preparation.—Powdered, ripe nux-vomica seeds are boiled well with dilute (0·1 per cent) hydrochloric acid, to extract the alkaloids as hydrochlorides. The liquid is filtered and the marc extracted with a further quantity of acid. The mixed filtrates are treated with a slight excess of milk of lime, and the precipitate, consisting of strychnine and brucine together with the excess of calcium hydroxide, is filtered off, washed, and extracted with boiling alcohol. The alcoholic solution is then evaporated and allowed to crystallise. The crystals, comprising brucine and strychnine, are filtered off and dried.

In order to free the product from brucine, 11 parts of the powdered, mixed alkaloids are heated to boiling with 60 parts of water, and dilute nitric acid is gradually added until the liquid is slightly acid, in order to oxidise the brucine. On cooling, strychnine nitrate separates out from the red liquid, and a further quantity may be obtained by concentration of the mother liquor.

The free alkaloid is obtained from the nitrate by dissolving in water, precipitating with ammonium hydroxide, filtering off, and recrystallising from boiling alcohol.

Properties.—Colourless prisms or a white crystalline powder. Soluble 1-7000 in water, forming an intensely bitter solution; soluble 1-150 in alcohol (90 per cent) and about 1-12 in boiling alcohol (90 per cent).

Tests for Impurities. *Metallic Compounds.*—On ignition, it should leave no appreciable ash.

Brucine (*Limit of*).—It should dissolve in concentrated sulphuric acid to form a colourless solution, which should not acquire more than a faint pink colour on addition of nitric acid.

According to the B.P.C., this test is best carried out by moistening the alkaloid with a mixture of equal volumes of nitric acid and water, when no coloration should be produced.

Strychninæ Hydrochloridum. *Strychnine Hydrochloride.*—This is prepared by suspending finely powdered strychnine in hot water and gradually adding hydrochloric acid until exactly neutral. The solution is filtered and evaporated on a water-bath to crystallisation.

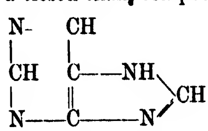
Properties.—Small, colourless prisms. The solubility in water was given in the 1898 Pharmacopœia as 1-35, but this has been altered in the 1914 edition to 1-60. Both the 1911 and the 1923 editions of the B.P.C. give the solubility as 1-35·5. Squire (1916 edition) gives the solubility as 1-43.

Tests for Impurities.—Test as described under Strychnina.

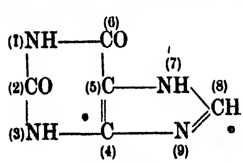
Quantitative Test.—The Pharmacopœia states that it should lose between 7 and 9 per cent of its weight when dried at 110° (equivalent to about $1\frac{1}{2}$ to 2 molecules of water of crystallisation). Both the 1911 and 1923 editions of the B.P.C. draw attention to the fact that the available evidence is in favour of the view that the salt contains $1\frac{1}{2}$ molecules of water of crystallisation. The 1914 Pharmacopœia retains, however, the formula $C_{21}H_{22}N_2O_2,HCl,2H_2O$.

Purine Derivatives

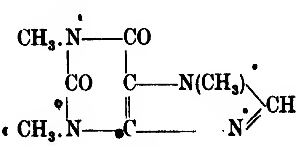
Purine, $C_5H_4N_4$, is a closed-chain compound of the formula



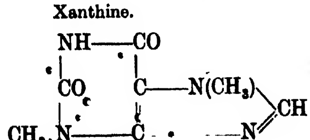
Purine is itself a substance of little importance, but it is of interest as being the parent of a group of important natural products, of which the chief are xanthine, caffeine, theobromine, and uric acid. The relationship of these compounds to purine and to each other will be seen from their structural formulæ :



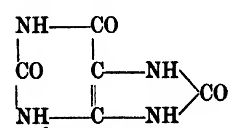
Xanthine.



Caffeine.



Theobromine.



Uric acid.

Caffeine, theine, 1, 3, 7-trimethyl xanthine, $C_8H_{10}N_4O_2$, is an alkaloid which occurs in tea, coffee, and guarana, and is usually obtained from tea.

Caffeine forms silky masses of colourless needles, containing 1 molecule of water of crystallisation. Soluble 1-80 in water. Melting-point, 235°. It is a very feeble base. Its aqueous solutions are neutral to litmus, and its salts are readily hydrolysed by water; the citrate, for example, is soluble 1-4 in hot water, but on further addition of water it undergoes hydrolysis, with separation of caffeine.

Caffeine can be detected by the very characteristic murexide test. A little of the sample is treated with a crystal of potassium chlorate and a few drops of concentrated hydrochloric acid, and the mixture evaporated to dryness on a water-bath. The reddish-brown residue is allowed to cool and treated with a drop of ammonium hydroxide, when a deep purple coloration is produced. This reaction is also given by theobromine and certain other purine derivatives.

Theobromine, 3, 7-dimethyl xanthine, $C_7H_8N_4O_2$, occurs in cocoa beans, and is a crystalline, sparingly soluble powder.

It resembles caffeine in chemical properties, being a very feeble base. At the same time it has some acidic properties, and forms unstable metallic salts, the metal displacing the hydrogen atom of the —NH group.

Theobrominæ et Sodii Salicylas. *Theobromine and Sodium Salicylate.*—This substance, known under the trade name of "diuretin", is a mixture of sodium salicylate, $C_6H_4(OH)COONa$, and the sodium derivative of theobromine, $NaC_7H_7N_4O_2$, in molecular proportions.

Preparation.—A solution of sodium hydroxide (1 part) in water (1 part) is diluted with 8 parts of alcohol (95 per cent). A portion of this solution is standardised by titration, and a volume of the solution, calculated as containing 20 parts of pure sodium hydroxide, is added to 100 parts of water. Theobromine (90 parts) is then added, and the mixture is warmed until solution is complete. This liquid is then mixed with a solution of 80 parts of sodium salicylate in 75 parts of water, and the whole filtered and quickly evaporated to dryness.

Uric acid, $C_5H_4N_4O_3$, cannot be termed an alkaloid, but on account of its close relationship to caffeine and theobromine it may be conveniently dealt with here. It is a most important product of animal metabolism, and is a normal constituent of urine.

Uric acid is a white crystalline powder, almost insoluble in water. It behaves like a weak dibasic acid, the hydrogen atoms of two of the —NH groups being displaceable by metals. The di-sodium salt is formed when uric acid is dissolved in aqueous sodium hydroxide, in which it is freely soluble. If sodium carbonate is employed only one hydrogen atom is displaced, the mono-sodium salt being produced.

OFFICIAL ALKALOIDS AND ALKALOIDAL SALTS

Alkaloid.	Principal Sources.	Official.
Aconitine	Aconitum Napellus	Aconitina, $C_{34}H_{45}NO_{11}$
Apomorphine	Prepared from morphine	Apomorphinæ Hydrochloridum, $(C_{17}H_{17}NO_2,HCl)_2,H_2O$
Atropine	Atropa Belladonna and other Solanaceous plants	Atropina, $C_{17}H_{23}NO_3$ Atropinæ Sulphas, $(C_{17}H_{23}NO_3)_2,H_2SO_4$
Benzamine	Synthetic	Benzaminæ Lactas, $C_{15}H_{21}NO_2,C_3H_6O_3$
Caffeine	Leaves of Camellia Thea and certain other plants	Caffeina, $C_8H_{10}N_4O_2,H_2O$ Caffeinæ Citras, $C_8H_{10}N_4O_2,C_6H_8O_7$
Cocaine	Erythroxylum Coca and its varieties	Cocaina, $C_{17}H_{21}NO_4$ Cocainæ Hydrochloridum, $C_{17}H_{21}NO_4,HCl$
Codeine	Opium, or prepared from morphine	Codeina, $C_{18}H_{21}NO_3,H_2O$ Codeinæ Phosphas, $C_{18}H_{21}NO_3,H_3PO_4,2H_2O$
Diamorphine	Prepared from morphine	Diamorphinæ Hydrochloridum, $C_{21}H_{23}NO_5,HCl,H_2O$
Homatropine	Prepared from tropine	Homatropinæ Hydrobromidum, $C_{16}H_{21}NO_3,HBr$
Hyoscine	Various Solanaceous plants	Hyoscinæ Hydrobromidum, $C_{17}H_{21}NO_4,HBr,3H_2O$
Hyoscyamine	Various Solanaceous plants	Hyoscyaminæ Sulphas, $(C_{17}H_{23}NO_3)_2,H_2SO_4,2H_2O$
Morphine	Opium	Morphinæ Acetas, $C_{17}H_{19}NO_3,C_2H_4O_2,3H_2O$ Morphinæ Hydrochloridum, $C_{17}H_{19}NO_3,HCl,3H_2O$ Morphinæ Tartras, $(C_{17}H_{19}NO_3)_2,C_4H_6O_6,3H_2O$
Pelletierine *	Punica Granatum	Pelletierinæ Tannas
Physostigmine	Physostigma venenosum	Physostigminæ Sulphas, $(C_{15}H_{21}N_3O_2)_2,H_2SO_4$
Pilocarpine	Pilocarpus Microphyllus and other species of Pilocarpus	Pilocarpinæ Nitras, $C_{11}H_{16}N_2O_2,HNO_3$
Quinine	Various species of Cinchona	Quininæ Hydrochloridum, $C_{20}H_{24}N_2O_2,HCl,2H_2O$ Quininæ Hydrochloridum Acidum, $C_{20}H_{24}N_2O_2,2HCl$ Quininæ Sulphas, $(C_{20}H_{24}N_2O_2)_2,H_2SO_4,7\frac{1}{2}H_2O$
Strychnine	Strychnos Nux-vomica and other species of Strychnos	Strychnina, $C_{21}H_{22}N_2O_2$ Strychninæ Hydrochloridum, $C_{21}H_{22}N_2O_2,HCl,2H_2O$
Theobromine	Theobroma Cacao	Theobrominæ et Sodii Salicylas

* mixture of Alkaloids.

CHAPTER XXXIX

THE ASSAY OF ALKALOIDAL DRUGS AND THEIR PREPARATIONS

THE amount of active constituent in crude vegetable drugs is liable to considerable variation in different samples, the variation being attributable to factors such as the age of the plant, the time of the year when collected, the soil, the climate, the method employed in drying, and the mode of cultivation. While in some cases it is possible to estimate the quality of a drug by its appearance, in many other and important instances little information can be obtained by inspection only, so that when a method can be devised whereby the quantity of active constituent in a drug or its preparation may be determined with accuracy, it is of great advantage to medicine. The methods employed in the determination of the amount of active constituent in drugs may be divided into three classes:

(1) *Chemical Methods.*—These are employed chiefly in the estimation of alkaloids, glucosides, and other definite chemical substances upon which the action of the drug depends, and which can be isolated from it without much difficulty.

(2) *Biochemical Methods.*—These comprise the testing of the actual effect which the drug or its preparation has upon living animals, and the methods are only employed when no satisfactory assay process has been found. An instance is the injection of preparations of ergot into fowls, the degree of gangrene produced in the comb affording an indication as to the activity of the preparation. In other cases—*e.g.* digitalis and strophanthus—a tincture is made from the drug, the alcohol evaporated, and the resulting aqueous liquid injected into the dorsal lymph sac of a frog of known weight. The results may be expressed in terms of the minimum quantity required to kill a frog of certain weight in a definite time; that is, in M.L.D. (minimum lethal dose) units.

(3) *Extractive Methods.*—An indication as to the quality of a drug may be obtained in some cases by exhausting the drug with a suitable menstruum, and either evaporating to dryness and weighing, or taking the specific gravity of the liquid obtained.

Of these methods the first are by far the most accurate and important for alkaloids, and they only will be treated of here.

General Method

The proportion of alkaloids present in a drug or preparation is usually determined by making use of the following general properties possessed by most of the members of this class of compounds:

(1) Alkaloids are usually sparingly soluble in water, but readily soluble in certain organic solvents.

(2) Alkaloids combine directly with acids to form salts, which are usually soluble in water but insoluble in organic solvents.

(3) Alkaloids are precipitated from solutions of their salts by alkalies.

The method adopted involves the use of so-called immiscible solvents, such as water with ether or water with chloroform, and is, in general, as follows, the operation being conducted in a separating funnel:

A definite weight or volume of the drug or preparation is taken and mixed with a suitable alkali, whereupon the alkaloids, which usually occur in the drug in combination with organic acids, are liberated.

An organic solvent such as ether is added, and the free alkaloid passes into solution in this.

The ethereal layer is separated and shaken with acidified water; whereupon the salt of the alkaloid is formed, and this dissolves in the water, any resinous or fatty substances remaining in the ether.

The aqueous layer is separated, mixed with ether, made alkaline, and shaken. The alkaloid passes into solution in the ether, which may be then separated and evaporated, the residual alkaloid being dried and weighed.

The method is marred by the following difficulties, and unless precautions be taken serious loss may occur:

(1) The organic solvents employed are often very appreciably soluble in water, so that some of the dissolved alkaloid may remain in the aqueous layer. This is overcome by extracting with not less than three separate quantities of organic solvent in turn, and mixing them after separation.

(2) Complications may occur through the presence of resins, fats, and other organic substances which dissolve in the organic solvent if the liquid be acid, but in the water if the liquid be alkaline (owing to the formation of resinates or soaps).

(3) When the liquids are agitated in the separating funnel and allowed to stand, emulsification may occur between the organic solvent and the water, rendering the complete separation of the liquids difficult. This emulsification may often be avoided by rotating and occasionally inverting the separating funnel instead of shaking vigorously. If emulsification has occurred it is sometimes possible to bring about separation by the addition of more organic solvent, or by gently stirring the liquids with a wire.[1]

[1] The small quantities of organic solvent prescribed in many of the pharmacopœial assay processes tend to bring about an undue amount of emulsification,

(4) When the lower layer is run off, some of the liquid is often retained in the stem of the separator owing to capillary attraction. This liquor should be washed out by adding more to the contents of the separator and running off without shaking.

(5) When an alkali is mixed with an acid liquid heat is often generated and the stopper of the separator may be blown out, with loss of some of the contents. For this reason it is advisable to allow the mixture to stand for a short time, or at the most to mix by gentle rotation of the separator, before commencing to shake.

The organic solvent used in an assay process must be one which is not more than slightly soluble in water, which will dissolve the alkaloid readily, and which is easily separated. The commonest organic solvents are chloroform, ether (or a mixture of these), benzene, amyl alcohol, petroleum spirit, and kerosene. The last two of these are not used in any of the pharmacopœial processes, but are often employed in the extraction of alkaloids on the large scale.

The alkali must be one that will liberate the alkaloid from its salt without decomposing it, and not readily form soaps with any fat or resin present. The best are sodium bicarbonate, sodium carbonate, and ammonium hydroxide, the last being especially useful on account of its volatility. Sodium hydroxide and potassium hydroxide are not so generally useful owing to their propensity to form soaps.

Preliminary Exercise

Carefully weigh about 0·3 gramme of a quinine salt and dissolve in water acidified with dilute sulphuric acid (p. 394).

Transfer to a stoppered separating funnel and add a *slight* excess of ammonium hydroxide solution. The alkaloid is precipitated. (If a large excess of ammonia is present, some of the quinine will remain in solution.)

Add to the contents of the separator 15 mils of chloroform; shake with a rotary motion for a minute, allow the liquid to separate, and run off the lower, chloroformic layer into a second separator. To ensure complete extraction add two further quantities, each of 10 mils of chloroform, and after shaking and allowing to separate, mix with the first quantity of chloroform. Remove any chloroform adhering to the inside of the tube of the funnel by adding another 5 mils of chloroform and running off, without shaking, into the second separator.

Wash the chloroform in the second separator free from ammonia by adding a few mils of water. Run off the chloroform and then the water, then return the chloroform to the separator and repeat the washing with more water.

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and although the same quantities are given in this book, they may be doubled at the discretion of the teacher.

Evaporate the chloroform in a tared dish on a water-bath in a fume cupboard. Dry the residue in a water-oven and weigh. Calculate the percentage found compared with the weight first taken.

Typical Assays

Cinchonæ Rubræ Cortex.—Red Cinchona Bark is the dried bark of the stem and branches of cultivated plants of *Cinchona succirubra*. When used for official purposes other than the preparation of alkaloids or their salts, it is required to yield from 5 to 6 per cent of total alkaloids, of which not less than one-half should consist of quinine and cinchonidine when determined by the following process:

Mix 10 grammes of the bark, dried at 100° and in No. 60 powder, with 6 grammes of calcium hydroxide; add 22 mils of water, mix intimately in a small porcelain dish, and set aside for an hour or two. The alkaloids, which occur in the bark in combination with quinic and cinchotannic acids, are released from their salts.

Transfer the mixture, which will now be dry and crumbly, to a large flask fitted with an upright Liebig's condenser (to act as a reflux). Add 130 mils of benzolated amylic alcohol,[1] boil for half an hour, and then decant the liquid on to a filter, leaving the sediment in the flask. Add more of the benzolated amylic alcohol to the sediment, boil, and decant as before; repeat this operation a third time, then transfer the contents of the flask to the filter and wash the sediment with more of the benzolated amylic alcohol until the liquid which percolates through ceases to give any precipitate with acidified Mayer's reagent (p. 388), showing that the whole of the alkaloids originally in the bark have been extracted by the organic solvent.

Introduce a portion of the collected filtrate, while still warm, into a stoppered glass separator, and add a mixture of 2 mils of diluted hydrochloric acid and 12 mils of water; shake well and allow to separate, running off the lower acid layer. Add a further quantity of water slightly acidified with hydrochloric acid, shake, and run off the lower acid layer. Repeat this until all the alkaloids have been extracted as hydrochlorides, as shown by testing with Mayer's reagent. Treat the remainder of the collected filtrate in the same way, taking convenient portions at a time.

Mix all the acid liquids obtained and carefully and exactly neutralise, while still warm, with Solution of Ammonia, and then concentrate by evaporation to a volume of 16 mils. Add to the concentrated solution about 1·5 grammes of sodium potassium tartrate dissolved in 3 mils of water, stir with a glass rod, and then

[1] *Benzolated amylic alcohol*:

Benzene, 3 parts by volume,
Amyl alcohol, 1 part by volume.
Mix: decant from any deposited water.

set aside for an hour. Collect the precipitate on a double filter, formed of two counterbalanced filter papers, wash, dry in a water-oven, and weigh.

The weight in grammes multiplied by 8 gives the percentage of quinine and cinchonidine in the bark. Of the weight of alkaloidal tartrate which has been obtained the alkaloid represents 8 parts and the tartrate radicle 2 parts, and as 10 grammes of the bark was originally taken, it is necessary to multiply by 8 to obtain the percentage of quinine and cinchonidine.

Mix the mother liquor and washings from the preceding process, which contain the soluble tartrates of quinidine and cinchonine, and introduce into a stoppered separator. Make alkaline by adding slight excess of ammonium hydroxide and shake with three successive portions of 10 mils of chloroform. Mix the chloroform solutions, which contain the liberated quinidine and cinchonine, evaporate to dryness on a water-bath, dry in an air-oven at 110°, and weigh. The weight in grammes multiplied by 10 and added to the percentage of quinine and cinchonidine previously determined, gives the percentage of total alkaloids.

Extractum Cinchonæ Liquidum.—Liquid Extract of Cinchona is required to contain 5 grammes of the alkaloids of red cinchona bark in 100 mils.

Introduce into a stoppered glass separator 5 mils of the liquid extract, 15 mils of benzolated amylic alcohol (footnote, p. 408), and 10 mils of N/1 alcoholic solution of potassium hydroxide. Shake well and set aside in a warm place for a few minutes, shaking occasionally, then allow the liquids to separate. The alkaloids, which are present in the extract as hydrochlorides (owing to the use of hydrochloric acid in their extraction from the bark), are liberated by the potassium hydroxide, and pass into solution in the benzolated amylic alcohol.

Pour off the clear upper layer into a second separator, and complete the removal of the alkaloids by shaking with two further portions of 15 and 10 mils of benzolated amylic alcohol.

Shake the mixed quantities of benzolated amylic alcohol with two portions, each of 5 mils, of water to remove traces of alkali, and reject the wash water.

Mix together 12 mils of diluted hydrochloric acid and 60 mils of water, and shake the benzolated amylic alcohol with successive portions of 30, 30, and 12 mils of this, drawing off the acid liquids, which contain the alkaloids in solution as hydrochlorides, into a separator.

Add to the acid liquid 15 mils of chloroform and distinct excess of ammonium hydroxide; shake vigorously, allow to separate, and draw off the chloroformic layer into a tared dish. Complete the extraction of the liberated alkaloids by shaking with further quantities of 10 mils of chloroform until the aqueous liquid in the separator no longer yields a precipitate when a few drops are

acidified with dilute sulphuric acid and tested with Mayer's reagent (p. 388).

Collect the chloroformic solutions of the alkaloids in a tared dish and allow to evaporate slowly; dry the residue in an air-oven at 110° and weigh. Since 5 mils of the extract were originally taken, the weight in grammes of the alkaloids, multiplied by 20, gives the weight in volume percentage of total alkaloids. (Limit of error 0·2 gramme in excess or defect in 100 mils of liquid extract.[1])

Tinctura Cinchonæ.—Tincture of Cinchona is required to contain 1 gramme of the alkaloids of red cinchona bark in 100 mils. The assay process is as just described for the liquid extract, using 10 mils of the tincture. (Limit of error 0·05 gramme in excess or defect in 100 mils of tincture.)

Tinctura Cinchonæ Composita.—Compound Tincture of Cinchona is required to contain 0·5 gramme of the alkaloids of red cinchona bark in 100 mils. The assay process is as described for the liquid extract, 20 mils being a suitable quantity to work upon. (Limit of error 0·05 gramme in excess or defect in 100 mils of tincture.)

Extractum Belladonnæ Liquidum.—Liquid Extract of Belladonna is required to contain 0·75 gramme of the alkaloids of belladonna root (chiefly hyoscyamine and atropine) in 100 mils.

The first step is to remove most of the fat and colouring matter from the extract by shaking with chloroform, the liquid being previously made acid so that the chloroform shall not extract any of the alkaloid as well. Introduce into a stoppered separator 10 mils of the liquid extract, 50 mils of water (to dilute the alcoholic liquid, which would otherwise mix with the chloroform), 2 mils of diluted sulphuric acid (to convert the alkaloids into water-soluble salts), and 10 mils of chloroform. Shake vigorously, allow to separate, and run off the lower, chloroformic layer into a second separator. Wash the chloroform with two successive portions of 10 mils of water acidified with dilute sulphuric acid, and add the washings to the contents of the first separator, rejecting the chloroform. The chloroform is washed in order to recover any traces of alkaloids which it may have extracted, owing to the fact that the liquids are not completely immiscible.

Make the acid liquid in the first separator distinctly alkaline with ammonium hydroxide and extract the liberated alkaloids by shaking with three successive portions, each of 10 mils of chloroform.

Mix the chloroformic solutions, wash by shaking in a separator with 10 mils of water, allow to separate, run off the lower layer into a titration flask, and set aside for the chloroform to evaporate.

Heat the residue on a water-bath for half an hour to remove the

[1] *Limit of Error.*—The average of a number of assays of the same sample of a drug or preparation should not deviate from the prescribed standard to a greater or less extent than that indicated by the "limit of error".

last traces of ammonia and any volatile basic substances, and then dissolve in 10 mils of N/20 sulphuric acid by aid of very gentle heat. Determine the amount of sulphuric acid which has combined with the alkaloids by titrating the excess with N/20 sodium hydroxide, using tincture of cochineal as indicator.

The chief alkaloids in belladonna root are atropine and hyoscyamine, which, being isomers (p. 392), have the same molecular weight—289·2. Both are monacid bases, so that the equation may be written:

$$H_2SO_4 + 2C_{17}H_{23}NO_3 = (C_{17}H_{23}NO_3)_2H_2SO_4,$$
$$98 \equiv 2 \times 289{\cdot}2,$$
$$1000 \text{ mils N/1 } H_2SO_4 \equiv 289{\cdot}2 \text{ grammes of alkaloids,}$$
$$1 \text{ mil N/20 } H_2SO_4 \equiv 0{\cdot}01446 \text{ gramme of alkaloids.}$$

(Limit of error 0·05 gramme in excess or defect in 100 mils of liquid extract.)

Extractum Ipecacuanhæ Liquidum.—Liquid Extract of Ipecacuanha is required to contain 2 grammes of the alkaloids of ipecacuanha root in 100 mils.

Introduce into a stoppered separator 5 mils of liquid extract, 4 mils of water, 1 mil of dilute sulphuric acid, and 10 mils of ether. Shake, and run off the ethereal solution. Repeat the shaking with 5 mils of ether and again separate. This process is to remove most of the fat, resin, and colouring matter. The water dilutes the alcohol (90 per cent) with which the extract is prepared—without this the extract would mix with the ether. The alkaloids are converted into sulphates and remain in the aqueous-alcoholic layer.

Mix the ethereal solutions and wash by shaking in a second separator with two successive portions, each of 5 mils, of water. Add the washings to the contents of the first separator and reject the ether. This washing is necessary in order to recover any alkaloid which may be taken into solution by the ether, owing to the fact that ether and water are miscible to some extent.

To the contents of the first separator add 10 mils of chloroform and slight excess of ammonium hydroxide. The liberated alkaloids dissolve in the chloroform. Shake, allow to separate, and filter the chloroform through a small filter paper into a tared dish. Repeat the shaking with two further quantities of chloroform, separate, and pass the chloroform through the filter into the dish; finally, wash the filter with more chloroform and collect the washings in the dish.

Evaporate the mixed chloroformic solutions of the alkaloids until the bulk is reduced to about 2 mils, add 5 mils of ether to facilitate the removal of the last traces of chloroform, evaporate, dry in a water-oven at a temperature not exceeding 80°, and weigh. (Limit of error 0·1 gramme in excess or defect in 100 mils of liquid extract.)

A more accurate result will be obtained if the quantities are

doubled throughout the process, 10 mils of liquid extract being operated upon instead of 5 mils.

Extractum Nucis Vomicæ Liquidum.—*Liquid Extract of Nux Vomica is required to contain 1·5 grammes of strychnine in 100 mils.*

Remove the alcohol from 10 mils of the liquid extract by evaporating to a syrupy consistence in a porcelain dish on a water-bath. Dissolve the residue in 10 mils of warm water and transfer to a separator, washing the dish with a further 10 mils of water.

Add to the contents of the separator 10 mils of chloroform and a solution of 5 grammes of sodium carbonate in 25 mils of water. Shake vigorously, and set aside until the liquids have separated—this may take some time—and then run off the chloroform. Repeat the operation with two further quantities of chloroform, and mix the three chloroformic solutions of strychnine and brucine.

Extract the alkaloids from the chloroform by shaking with three successive portions, each of 10 mils, of N/1 sulphuric acid. Mix the acid solutions of strychnine and brucine sulphates in another separator. Make alkaline with ammonium hydroxide, and transfer the precipitated strychnine and brucine to chloroform by shaking with successive quantities of 10, 5, and 5 mils of this liquid.

Collect the chloroformic solutions in a small flask and evaporate off the chloroform.

The liquid extract is being assayed for strychnine only, and the next step is designed to oxidise the brucine into a ketonic compound which is insoluble in chloroform. To this end dissolve the residue of alkaloids in 15 mils of 3 per cent sulphuric acid, and warm the solution to 50° ; then add 3 mils of a mixture of equal volumes of nitric acid and water, and set aside for ten minutes. The decomposition of the brucine is shown by the formation of a characteristic deep crimson colour.

Transfer the crimson solution to a separator, rinsing the flask with a little water, make alkaline with sodium hydroxide solution, and extract the precipitated strychnine by shaking with three portions of 10, 5, and 5 mils of chloroform.

Wash the mixed chloroformic solutions free from alkali by shaking in another separator with 5 mils of water. Run off the chloroform into a tared dish and allow to evaporate on a water-bath, adding towards the end of the evaporation 5 mils of alcohol (90 per cent) in order to prevent loss by decrepitation.

Dry the residue in a water-oven and weigh. The weight in grammes, multiplied by 10, gives the percentage *w/v* of strychnine. (Limit of error 0·05 gramme in excess or defect in 100 mils of extract.)

Extractum Nucis Vomicæ Siccum —Dry Extract of Nux Vomica is required to contain 5 grammes of strychnine in 100 grammes. The dry extract may be assayed by mixing 3 grammes with an equal quantity of sand, packing in a percolating tube, and exhausting by percolation with alcohol (70 per cent). The resulting liquid may

then be assayed as described for Extractum Nucis Vomicæ Liquidum. (Limit of error 0·2 gramme in excess or defect in 100 grammes of extract.)

Tinctura Nucis Vomicæ.—Tincture of Nux Vomica is required to contain 0·125 gramme of strychnine in 100 mils. It may be assayed by the process described for Extractum Nucis Vomicæ Liquidum, evaporating about 100 mils to a syrupy consistence. (Limit of error 0·005 gramme in excess or defect in 100 mils of tincture.)

Opium.—Opium is the juice obtained by incision from the unripe capsules of *Papaver somniferum*, inspissated by spontaneous evaporation.

When used for official purposes other than the preparation of the alkaloids or their salts, opium must be of such a strength that, when dried and powdered, the resulting powder, dried at 60°, yields not less than 9·5 per cent and not more than 10·5 per cent of anhydrous morphine. Opium yielding when dried more than 10 per cent of anhydrous morphine, must be diluted to that percentage either with powdered milk-sugar or with an opium containing when dried between 7·5 and 10 per cent of anhydrous morphine.[1]

Triturate together 8 grammes of opium in No. 50 powder, dried at 60°, and 2 grammes of freshly prepared calcium hydroxide with 20 mils of water in a mortar until a uniform mixture results. Add 60 mils of water and set aside for half an hour, with occasional stirring. The alkaloids of the opium, which occur in combination as meconates and sulphates, are liberated; insoluble calcium meconate and sulphate are precipitated, but the morphine and narcotine, which are soluble in calcium hydroxide solution, remain in solution.

Filter off 51 mils of the liquid (representing 5 grammes of opium, since 8 grammes were mixed with 80 mils of water, 1 mil extra being taken to allow for increase of bulk due to extractive matter from the opium), collecting the filtrate in a narrow cylinder, such as a stoppered 100-mil measuring cylinder. Add to the liquid 5 mils of alcohol (90 per cent) and 25 mils of ether; shake, and add 2 grammes of ammonium chloride. Shake well and frequently during half an hour, then set aside for twelve hours. The ammonium chloride interacts with the lime, with liberation of ammonia, and this precipitates the morphine (insoluble in ether), its crystallisation being assisted by the alcohol. The narcotine is kept in solution by the ether.

Counterbalance two small filter papers; place one within the other in a small funnel so that the triple fold of one is superimposed upon the single fold of the other. Wet them with ether, remove

[1] Any suitable variety of opium may be employed for the preparation of the tincture and extract provided that, when dry, it contains not less than 7·5 per cent of anhydrous morphine.

the ethereal layer of the liquid in the cylinder as completely as possible by means of a small pipette, and pass the ether through the filter. Add a further quantity of 10 mils of ether to the contents of the cylinder in such a way as to rinse its sides, and transfer this ether to the filter by means of the pipette. Then wash the filter with 5 mils of ether, added slowly, and in small portions. In this way all the narcotine is removed.

After allowing the filter to dry pour upon it the contents of the cylinder and collect the granular precipitate of morphine. When all the liquid has passed through, wash the remainder of the morphine from the cylinder with morphinated water,[1] using a rubber-tipped glass rod, until the whole has been removed, and wash the filter with morphinated water until the washings are free from colour. Morphinated water is employed in order that no morphine shall be dissolved.

Allow the filter to drain and dry it, first in a water-oven at 60° and finally for two hours in an air-oven at 115°. Weigh the crystals in the inner filter, counterbalancing by the outer filter. Make a note of the weight. Then determine what proportion of this weight consists of pure anhydrous morphine by dissolving 0·2 gramme of the crystals in 10 mils of N/10 sulphuric acid and back titrating the excess of acid with N/10 sodium hydroxide, using methyl orange as indicator[2]:

$$H_2SO_4 + 2C_{17}H_{19}NO_3 = (C_{17}H_{19}NO_3)_2H_2SO_4,$$
$$98 \equiv 2 \times 285,$$
$$1000 \text{ mils N/1 } H_2SO_4 \equiv 285 \text{ grammes anhydrous morphine},$$
$$1 \text{ mil N/10 } H_2SO_4 \equiv 0{\cdot}0285 \text{ gramme anhydrous morphine}.$$

The weight of pure anhydrous morphine obtained (calculated from the titration) plus 0·051 gramme (the average loss of morphine during the process, owing to its slight solubility in ether) is the weight contained in 5 grammes of the opium. (Limit of error 0·5 gramme in 100 grammes of opium.)

Extractum Opii Siccum.—Dry Extract of Opium is required to contain 20 grammes of anhydrous morphine in 100 grammes. It is tested by the process described under Opium. (Limit of error 1 gramme in excess or defect in 100 grammes of the extract.)

Tinctura Opii. — Tincture of Opium is required to contain 1 gramme of anhydrous morphine in 100 mils.

The process is similar to that described for Opium (*q.v.*), with certain modifications.

[1] *Morphinated Water.*—A saturated solution of morphine in chloroform water, obtained by maintaining excess of morphine in contact with the chloroform water for seven days, at a temperature of 15·5°, shaking occasionally, and then filtering. Solubility of morphine = 1-1,000 (about).

[2] For this titration, cochineal is a more suitable indicator than methyl orange.

Evaporate 40 mils to 10 mils in a dish on a water-bath and then transfer to a small measuring cylinder. Add 1 gramme of freshly slaked lime. Rinse the dish with sufficient water, so that when the rinsings are added to the contents of the cylinder the mixture has a volume of 41 mils. Set aside for half an hour, with occasional stirring.

Filter off 25 mils of the liquid (corresponding to 25 mils of the tincture) through a plaited filter of about 10 cms. diameter into a stoppered cylinder, add 2·5 mils of alcohol (90 per cent) and 15 mils of ether. Shake, then add 1 gramme of ammonium chloride, and set aside for half an hour with frequent shaking.

From this point the process is exactly as described for Opium, except that 8 mils of ether are used to rinse the cylinder instead of 10 mils. The weight to be added to allow for the average loss of morphine is 0·025 gramme. (Limit of error 0·05 gramme in excess or defect in 100 mils of tincture.)

Extractum Opii Liquidum.—Liquid Extract of Opium is required to contain 0·75 gramme of anhydrous morphine in 100 mils. It is tested by the process described under Tinctura Opii. (Limit of error 0·05 gramme in excess or defect in 100 mils of liquid extract.)

Other Alkaloidal Assays

The following are assayed by methods similar to those previously described:

Belladonnæ Folia.
Tinctura Belladonnæ.
Extractum Belladonnæ Siccum.
Extractum Hyoscyami.
Ipecacuanhæ Radix.
Aconiti Radix.
Tinctura Aconiti.
Linimentum Aconiti.
Extractum Hydrastis Liquidum.
Caffeinæ Citras.

APPENDIX

ANALYTICAL TABLES

TABLES FOR THE IDENTIFICATION OF INORGANIC SUBSTANCES

THE colour and general appearance of the substance should be noted, and also its reaction towards moistened litmus paper.

Copper	salts are generally	blue or green.
Iron	,, ,,	green or brown.
Chromium	,, ,,	green.
Manganese	,, ,,	pale pink.
Nickel	,, ,,	green.
Cobalt	,, ,,	pink.
Chromates	,,	yellow.
Dichromates	,,	orange.
Permanganates	,,	dark purple.

The oxides and/or sulphides of the following metals are coloured:

Lead, mercury, silver, copper, bismuth, cadmium, arsenic, antimony, tin, iron, chromium, manganese, nickel, and cobalt.

PRELIMINARY TESTS

Heat to redness in a dry ignition tube.

A few substances (mostly oxides) undergo temporary changes in colour.

Many hydrated salts undergo changes in colour due to loss of water of crystallisation.

Ammonium salts, and most compounds of mercury and arsenic, sublime.

Charring, or evolution of inflammable vapours, indicates an organic substance (*see* Organic Tables).

The following gases or vapours may be evolved:

Water Vapour.—Salts containing water of crystallisation, and certain hydroxides and basic salts.

Oxygen (rekindles a glowing splint).—Certain oxides, also nitrates, chlorates, bromates, iodates, and certain other oxy-salts.

Nitrous Oxide (rekindles a glowing splint).—Ammonium nitrate.

Nitrogen Peroxide (brown fumes).—All nitrates and nitrites, except those of the alkali metals and ammonium.

Carbon Dioxide (turns lime water milky).—Many carbonates and bicarbonates.

Sulphur Dioxide (turns potassium dichromate paper green).—Some sulphates and sulphites.

Sulphur Vapour.—Thiosulphates and polysulphides.

Ammonia (alkaline to litmus).—Certain ammonium salts.

Flame Test.—To be applied to the substance moistened with concentrated hydrochloric acid.

Grey or bluish-grey . .	Lead, arsenic, antimony, tin.
Bluish-green	Copper.
Apple green	Barium.
Brick-red	Calcium.
Crimson	Strontium or lithium.
Lilac (crimson through indigo prism)	Potassium.
Bright yellow (invisible through indigo prism) .	Sodium.

Borax Bead Test.—Introduce a trace of the substance into a fused borax bead on a platinum wire, and reheat in the outer portion of a bunsen flame (this test need only be applied if the original substance is coloured).

Bluish-green bead . . .	Copper.
Bright green bead . . .	Chromium.
Yellow bead	Iron.
Deep amethyst bead . .	Manganese.
Deep blue bead . . .	Cobalt.
Brown bead	Nickel.

Action of Sodium Carbonate solution.

Ammonia evolved, in the cold or on gently warming.—Ammonium salt.

Action of Dilute Sulphuric Acid.—The following gases or vapours may be evolved:

Carbon Dioxide.—Carbonate or bicarbonate.

Hydrogen Sulphide (blackens lead acetate paper).—Sulphide.

Hydrogen Sulphide, with Precipitation of Sulphur.—Polysulphide.

Sulphur Dioxide.—Sulphite.

Sulphur Dioxide, with Precipitation of Sulphur.—Thiosulphate.

Nitrogen Peroxide.—Nitrite.

Chlorine.—Hypochlorite.

Odour of Hydrocyanic acid.—Cyanide (*see* Organic Tables).

Odour of Acetic Acid, on warming.—Acetate (*see* Organic Tables).

Action of Concentrated Sulphuric Acid.

Charring on warming, or evolution of carbon monoxide or

carbon dioxide (other than carbon dioxide from a carbonate) indicates an organic substance (*see* Organic Tables).

The following gases or vapours may be evolved, in addition to those mentioned in the previous test:

Hydrogen Fluoride (colourless fuming gas which attacks glass).—Fluoride.

Hydrogen Chloride (colourless fuming gas).—Chloride. Confirm by adding manganese dioxide and warming, when chlorine will be evolved.

Hydrogen Bromide (colourless fuming gas) and *Bromine Vapour*.—Bromide.

Iodine Vapour.—Iodide.

Nitric Acid Fumes.—Nitrate. Confirm by adding metallic copper, when nitrogen peroxide will be evolved. Also, apply the brown ring test (p. 35).

Chlorine Peroxide (explosive yellow gas).—Chlorate.

EXAMINATION FOR METALS

Prepare a solution of the substance, trying the following solvents in turn:

Water.
Dilute hydrochloric acid.
Concentrated hydrochloric acid.
Dilute nitric acid.
Concentrated nitric acid.
A mixture of concentrated hydrochloric acid (4 parts) and concentrated nitric acid (1 part).[1]

If any nitric acid has been used in effecting solution, it must be removed, before proceeding further, by evaporating nearly to dryness, adding concentrated hydrochloric acid, evaporating nearly to dryness again, and finally diluting with water.

[1] If the substance is insoluble in all of these solvents, it is probably one of the following:

Lead, barium, or strontium sulphates.
Silver chloride, bromide, or iodide.
Stannic oxide or sulphide.
Ignited aluminium, chromium, or ferric oxides.
Calcium fluoride.
Silica or an insoluble silicate.

These substances may be identified in the insoluble portion of the substance by special methods. A common way of dealing with an insoluble substance is to fuse it with about five times its weight of sodium carbonate or fusion mixture, allow to cool, boil the residue with water, and filter. During the fusion double decomposition takes place, as, for example:

$$BaSO_4 + Na_2CO_3 = BaCO_3 + Na_2SO_4.$$

The filtrate is examined for acid radicles, and the residue, after washing with water, is dissolved in dilute hydrochloric acid and examined for metals.

Examine the solution as follows:

TABLE FOR THE SEPARATION OF METALS INTO GROUPS

<table>
<tr><td colspan="7">Add to the solution dilute hydrochloric acid. Cool well, and filter.</td></tr>
<tr><td rowspan="5">Residue.—Silver, mercurous, lead. Examine by table for Group I.</td><td colspan="6">Filtrate.—Dilute, warm, and pass hydrogen sulphide.</td></tr>
<tr><td colspan="2">Residue.—Wash well, warm with yellow ammonium sulphide for a few minutes, and filter.</td><td colspan="4">Filtrate.—Boil to expel hydrogen sulphide, add a few drops of nitric acid, and boil again. Add ammonium chloride and excess of ammonium hydroxide. Filter.</td></tr>
<tr><td rowspan="3">Residue.—Lead,[1] mercuric, bismuth, copper, cadmium. Examine by table for Group IIa.</td><td rowspan="3">Filtrate.—May contain: arsenic, antimony, tin. Examine by table for Group IIb.</td><td rowspan="3">Residue.—Aluminium, chromium, iron, or an insoluble phosphate.[2] Examine by table for Group III.</td><td colspan="3">Filtrate.—Add ammonium sulphide, and filter.</td></tr>
<tr><td rowspan="2">Residue.—Zinc, manganese, nickel, cobalt. Examine by table for Group IV.</td><td colspan="2">Filtrate.—Add ammonium carbonate, and filter.</td></tr>
<tr><td>Residue.—Barium, strontium, calcium. Examine by table for Group V.</td><td>Filtrate.—May contain: magnesium, lithium, sodium, potassium. Examine by table for Group VI.</td></tr>
</table>

SEPARATION OF METALS OF GROUP I.

<table>
<tr><td colspan="3">Wash the precipitate with cold water. Boil with water, and filter hot.</td></tr>
<tr><td colspan="2">Residue.—Wash with boiling water, and pour warm ammonium hydroxide over the filter.</td><td rowspan="2">Filtrate.—Small needle-like crystals deposited on cooling.—Lead. Confirm by heating to boiling again and adding potassium chromate. Yellow precipitate.—
Lead.</td></tr>
<tr><td>Residue.—Black.—
Mercurous.</td><td>Filtrate.—Acidify with nitric acid. White precipitate.—
Silver.</td></tr>
</table>

[1] When lead is present, a little is always precipitated in this group, as lead chloride is slightly soluble in cold water.

[2] Manganese is sometimes precipitated in this group, and should always be tested for unless the precipitate is white.

Separation of Metals of Group IIA.

<table>
<tr><td colspan="5">Wash the precipitate, boil with dilute nitric acid, and filter.</td></tr>
<tr><td rowspan="4">Residue.—Black.—Mercuric. Confirm by dissolving in a mixture of concentrated hydrochloric and nitric acids, diluting well, and adding stannous chloride. White precipitate.—Mercuric.</td><td colspan="4">Filtrate.—Add dilute sulphuric acid, allow to stand a few minutes, and filter.</td></tr>
<tr><td rowspan="3">Residue.—White.—Lead.</td><td colspan="3">Filtrate.—Add excess of ammonium hydroxide, warm, and filter.</td></tr>
<tr><td rowspan="2">Residue.—White.—Bismuth. Dissolve in dilute hydrochloric acid, and pour into about a litre of water. White turbidity.—Bismuth.</td><td colspan="2">Filtrate.—If blue, copper is present. Divide into two parts.</td></tr>
<tr><td>I. Acidify with acetic acid and add potassium ferrocyanide. Brown precipitate or coloration.—Copper.</td><td>II. If copper be present, add potassium cyanide until colourless. Pass hydrogen sulphide. Yellow precipitate.—Cadmium.</td></tr>
</table>

Separation of Metals of Group IIB.

<table>
<tr><td colspan="3">Acidify the solution with dilute hydrochloric acid. A yellow or orange precipitate (other than sulphur, which is very pale yellow) shows the presence of arsenic, antimony, or tin. Boil the precipitate with concentrated hydrochloric acid, and filter.</td></tr>
<tr><td rowspan="2">Residue.—Yellow.—Arsenic. Confirm by Fleitmann's test (p. 143).</td><td colspan="2">Filtrate.—Make slightly alkaline with ammonium hydroxide, add solid oxalic acid, and boil. Pass hydrogen sulphide, and filter.</td></tr>
<tr><td>Residue.—Orange.—Antimony.</td><td>Filtrate.—Make alkaline with ammonium hydroxide, acidify with acetic acid, and boil. Pass hydrogen sulphide. Brownish-yellow precipitate.—Tin.</td></tr>
</table>

Separation of Metals of Group III.

<table>
<tr><td colspan="3">A small portion of the precipitate must be tested for phosphate by dissolving in dilute nitric acid, adding excess of ammonium molybdate solution, and warming. A canary-yellow precipitate shows the presence of phosphate. If phosphate is present, examine the main portion of the precipitate by the next table. If phosphate is absent, boil the main portion of the precipitate with sodium hydroxide solution, and filter.</td></tr>
<tr><td colspan="2">Residue.—Suspend in water, add excess of sodium peroxide, in small quantities at a time, boil, and filter.</td><td rowspan="2">Filtrate.—Add excess of ammonium chloride, and boil. White precipitate.—Aluminium.</td></tr>
<tr><td>Residue.—Brown.—Iron. Dissolve in dilute hydrochloric acid, and add potassium ferrocyanide. Prussian blue precipitate.—Iron.
Test original substance for Fe'' and Fe'''.</td><td>Filtrate.—If yellow, chromium is present. Acidify with acetic acid and add lead acetate. Yellow precipitate.—Chromium.</td></tr>
</table>

Treatment of Group III. Precipitate when Phosphate is present

<table>
<tr><td colspan="2">Test a small portion of the precipitate for iron by dissolving in dilute hydrochloric acid and adding potassium ferrocyanide. A Prussian blue precipitate shows presence of iron. Dissolve the remainder of the precipitate in the least possible quantity of dilute hydrochloric acid, and add excess of ammonium acetate, followed by ferric chloride solution, drop by drop, until the liquid is red. Boil well, and filter.</td></tr>
<tr><td>Residue.—Consists of basic ferric acetate and ferric phosphate, with, possibly, aluminium or chromium. Examine for aluminium and chromium by the previous table.</td><td>Filtrate.—Add ammonium chloride and excess of ammonium hydroxide, filter if necessary, and examine the filtrate for metals of Groups IV., V., and VI.</td></tr>
</table>

Separation of Metals of Group IV.

<table>
<tr><td colspan="4">Wash the precipitate, shake well with cold, very dilute, hydrochloric acid, and filter.</td></tr>
<tr><td colspan="2">Residue.—Dissolve in concentrated hydrochloric acid with a little potassium chlorate. Evaporate the solution just to dryness. Dissolve the residue in water, add potassium cyanide, drop by drop, until the precipitate first formed just redissolves. Boil, add excess of sodium hydroxide and bromine water, boil again, and filter.</td><td colspan="2">Filtrate.—Boil to expel hydrogen sulphide. Cool, add excess of sodium hydroxide, and filter.</td></tr>
<tr><td>Residue.—Black.—Nickel. Fuse in a borax bead. Brown bead.—
Nickel.</td><td>Filtrate. — Evaporate just to dryness, and fuse the residue in a borax bead. Blue bead.—
Cobalt.</td><td>Residue. —Flesh-coloured or brown. —Manganese. Boil with excess of lead peroxide and concentrated nitric acid, dilute, and allow to settle. Purple supernatant liquid.—
Manganese.</td><td>Filtrate. — Pass hydrogen sulphide. White or dirty white precipitate.—
Zinc.</td></tr>
</table>

Separation of Metals of Group V.

<table>
<tr><td colspan="3">Wash the precipitate, dissolve in dilute acetic acid, add potassium chromate, and filter.</td></tr>
<tr><td rowspan="2">Residue.—Yellow.—
Barium.</td><td colspan="2">Filtrate.—Divide into two parts.</td></tr>
<tr><td>Part I.—Add calcium sulphate solution, and allow to stand. Small white precipitate.—
Strontium.</td><td>Part II.—Add dilute sulphuric acid, warm, and allow to stand. Filter if necessary, make the filtrate alkaline with ammonium hydroxide, and add ammonium oxalate. White precipitate.—
Calcium.</td></tr>
</table>

SEPARATION OF METALS OF GROUP VI.

<table>
<tr><td colspan="3">Divide the solution into two parts.</td></tr>
<tr><td colspan="2">Part I.—Add sodium phosphate. Shake well, and filter.</td><td rowspan="2">Part II.—Evaporate to dryness, and apply the flame test to the residue.
Crimson flame, invisible through indigo prism.—
Lithium.
Lilac flame, crimson through indigo prism.—
Potassium.
Bright yellow flame, invisible through indigo prism.—
Sodium.</td></tr>
<tr><td>Residue.—
White.—
Magnesium.</td><td>Filtrate.—Add excess of sodium hydroxide, and boil well. White precipitate.—
Lithium.</td></tr>
</table>

FINAL EXAMINATION FOR ACID RADICLES

Boil the original substance with sodium carbonate solution, and filter. Divide the filtrate into two parts and apply the following tests:

PART I. OF THE SOLUTION

<table>
<tr><td colspan="2">Acidify with dilute nitric acid, add excess of silver nitrate, and filter cold.</td></tr>
<tr><td>Residue.—White. May contain:
Chloride, Bromide, Iodide } Insoluble in boiling concentrated nitric acid.
Bromate, Iodate, Cyanide, Oxalate } Soluble in boiling concentrated nitric acid.
All the above precipitates are white, and readily soluble in dilute ammonium hydroxide, with the following exceptions:
Bromide.—Pale yellow, and sparingly soluble.
Iodide.—Yellow, and almost insoluble.</td><td>Filtrate.—Add ammonium hydroxide, drop by drop, until a precipitate is produced.
White precipitate.—Borate.
Oxalate.
Tartrate.
Yellow precipitate.—Phosphate.
Arsenite.
Brown precipitate.—Arsenate.
Brownish-red precipitate.—Chromate.
Confirm borate by mixing the original substance with a few drops of concentrated sulphuric acid and alcohol, and applying a light to the mixture. If borate is present, the flame has a green tinge.</td></tr>
</table>

PART II. OF THE SOLUTION

<table>
<tr><td colspan="2">Acidify with dilute hydrochloric acid, add excess of barium chloride, boil, and filter.</td></tr>
<tr><td>Residue.—
White.—
Sulphate.</td><td>Filtrate.—Cool, and add excess of ammonium hydroxide. The following may be precipitated:
Borate (white), Phosphate (white), Arsenite (white), Arsenate (white), Tartrate (white) } Soluble in dilute acetic acid.
Oxalate (white) Sparingly soluble in dilute acetic acid.
Fluoride (white), Chromate (yellow) } Insoluble in dilute acetic acid.</td></tr>
</table>

SCHEME FOR THE IDENTIFICATION OF CERTAIN ORGANIC COMPOUNDS[1]

THE substance may be either a solid or a liquid. If a liquid, it is probably one of the following: methyl alcohol, ethyl alcohol, solution of formaldehyde, acetone, acetic acid, chloroform, glycerin, hydrocyanic acid, or an aqueous solution of an organic substance.

A. The Substance is a Liquid

Evaporate a portion to dryness, at a temperature not exceeding 130°.—Note any odour evolved during this process, and the nature of the residue, if any.

If the residue is a viscous, practically odourless liquid, it is glycerin. Confirm by heating strongly with an equal weight of potassium hydrogen sulphate, when the characteristic, pungent odour of acrolein (p. 283) is evolved.

If the residue is a viscous liquid, possibly solidifying to a crystalline mass on cooling, and having the characteristic odour of phenol, examine by Section B.

If the characteristic odour of formaldehyde is evolved during the process of evaporation, and a white, amorphous solid residue remains which sublimes on strongly heating, the liquid is probably a solution of formaldehyde, the solid residue being paraformaldehyde formed by polymerisation during the process of evaporation. Confirm by tests given on p. 233.

Any solid residue obtained, other than paraformaldehyde, must be examined by Section B.

If the liquid is completely volatile below 130°, examine as follows:

Carefully note the odour, and, if the presence of acetic acid, chloroform, or hydrocyanic acid is suspected, apply the tests for acetates (p. 248), chloroform (p. 271), or cyanides (p. 304). If none of these is present the substance must be either methyl alcohol, ethyl alcohol, or acetone. Apply the following tests:

[1] As required by the syllabus for the C— Examination.

Warm a little of the liquid with a solution of potassium dichromate acidified with dilute sulphuric acid.—Reduction of the dichromate shows the presence of methyl or ethyl alcohol. In the case of ethyl alcohol, the characteristic odour of acetaldehyde will be observed.

Warm a few drops of the liquid with about 5 mils of sodium carbonate solution and a crystal of iodine.—A yellow crystalline precipitate, with the characteristic odour of iodoform, shows the presence of ethyl alcohol or acetone.

Shake the liquid with an equal volume of a cold, concentrated, freshly prepared solution of sodium bisulphite.—A white crystalline precipitate, separating with some development of heat, shows the presence of acetone.

The identity of the liquid may be finally confirmed by a determination of its boiling-point.

B. The Substance is a Solid

If in deliquescent, colourless crystals, having the characteristic odour of phenol, confirm by tests given on p. 347.

Apply the following tests :

Heat to redness in a dry ignition tube :

Cyanogen evolved (burns with a peach-coloured flame).—Mercuric or silver cyanide.

Odour of Phenol evolved.—Salicylate.

Charring, with Odour of Burnt Sugar.—Sucrose, glucose, lactose, starch, tartaric acid or a tartrate, salicin.

Charring, with Odour of Singed Hair.—Alkaloid.

Most other organic compounds char on ignition.

Warm with dilute sulphuric acid :

Odour of Hydrocyanic Acid evolved.—Cyanide. Confirm by tests given on p. 304.

Odour of Acetic Acid evolved.—Acetate. Confirm by tests given on p. 248.

Treat with concentrated sulphuric acid :

Deep Red Colour produced in the Cold.—Salicin. Confirm by tests given on p. 382.

Considerable Charring on gently warming.—Sucrose, glucose, lactose, starch, tartrate.

Charring on boiling.—Citrate, salicylate, alkaloid.

Carbon Monoxide evolved (no charring).—Cyanide.

Carbon Monoxide and Carbon Dioxide evolved (no charring).—Oxalate.

Tests for Metals

If, on ignition in a free access of air (on a crucible lid or in an open crucible), the substance burns away without residue, it is

unnecessary to test for metals other than mercury, arsenic, antimony and the basic radicle ammonium.

If a residue remains after ignition, test the original substance for metals by the ordinary methods of group analysis, with the following modification. After removal of Group II. metals by means of hydrogen sulphide, evaporate the filtrate to dryness, and ignite the residue in order to decompose organic matter; allow to cool, add dilute hydrochloric acid, boil, filter, and employ the filtrate for testing for metals of the remaining groups. If metals of Groups I. and II. are absent, the original substance may be ignited, the residue boiled with dilute hydrochloric acid and filtered, and the filtrate employed for testing for metals.

Tests for Alkaloids

Apply the general tests for alkaloids (p. 388), and, if an indication is given, apply individual tests for cocaine (p. 390), morphine (p. 397), quinine (p. 394), and strychnine (p. 400).

Alkaloids may be present either in the free state or as salts. If an alkaloid has been found, boil the original substance with aqueous sodium carbonate, cool, filter, and test the filtrate for the following acidic radicles: chloride, bromide, sulphate, nitrate, phosphate, acetate, tartrate, citrate, salicylate.

Tests for Organic Acids

<table>
<tr><td colspan="4">Boil about 2 grammes of the substance with about 10 mils of concentrated sodium carbonate solution, and filter. Cool the filtrate thoroughly, acidify with acetic acid, and filter off any precipitate.</td></tr>
<tr><td rowspan="3">Residue.—Of benzoic or salicylic acid shows presence of benzoate or salicylate. Wash with a little cold water, dissolve in ammonium hydroxide, boil to expel excess of ammonia, cool, and add ferric chloride. Buff precipitate.—Benzoate. Confirm by tests given on p. 360. Violet coloration.—Salicylate. Confirm by tests given on p. 365.</td><td colspan="3">Filtrate.—Add calcium chloride, and filter.</td></tr>
<tr><td rowspan="2">Residue.—White.—Oxalate.</td><td colspan="2">Filtrate.—Make just alkaline with ammonium hydroxide, shake well, allow to stand, and filter.</td></tr>
<tr><td>Residue.—White.—Tartrate.</td><td>Filtrate.—Boil for two minutes. White crystalline precipitate.—Citrate.</td></tr>
</table>

Tests for Carbohydrates

Boil with a little Water.—Jelly-like mucilage produced.—Starch. Confirm by cooling and adding a trace of iodine, when a deep blue colour is produced.

Shake with water, filter if necessary, add Fehling's solution to the filtrate, and heat nearly to boiling. Red precipitate.—Glucose, lactose. Confirm by tests given on pp. 316, 321.

Boil for five minutes with dilute hydrochloric acid, make alkaline with sodium hydroxide, filter if necessary, add Fehling's solution to the filtrate, and heat nearly to boiling. In the absence of glucose or lactose, a red precipitate shows the presence of sucrose or starch (pp. 320, 323).

NOTES ON THE IDENTIFICATION OF ORGANIC COMPOUNDS IN GENERAL[1]

It is not feasible to devise a general systematic scheme for the identification of organic compounds. The usual procedure is to apply a few simple tests, and then to follow up any indications thus obtained as to the chemical nature of the substance. It will therefore be seen that the method of attack, after a few preliminary experiments, will vary considerably with different compounds.

Physical Properties.—In many cases the type or class to which a compound belongs can be ascertained from the odour, as in the case of hydrocarbons (compare petroleum and benzene), esters, halogen derivatives of hydrocarbons, nitro-compounds, monohydric phenols, amines (aliphatic and aromatic), and cyanides.

Solubility in Water.—All hydrocarbons are insoluble. If hydrogen is displaced by groups such as —OH, $—NH_2$, —COOH, $—CO.NH_2$, $—SO_3H$, >CO, or —CHO, the product may be soluble, but the effect produced depends—

(*a*) On the number of such groups which have displaced hydrogen atoms (compare $C_6H_5.OH$ and $C_6H_4(OH)_2$).

(*b*) On the molecular weight of the remaining hydrocarbon radicle (compare $CH_3.OH$ and $C_5H_{11}.OH$).

Halogen derivatives of hydrocarbons, ethers, esters, nitro-compounds, and cyanides are practically insoluble in water, unless they also contain one of the above groups, or have a relatively low molecular weight.

Boiling-point.—The boiling-point of a substance, taken in conjunction with the behaviour towards water, affords some idea of the molecular weight, and the following boiling-points should be committed to memory as a guide: ether (35°), acetone (56°), ethyl alcohol (78°), ethyl acetate (78°), benzene (80°), phenol (183°), aniline (183°), and nitrobenzene (208°).

The boiling-point may be observed fairly accurately in a test-tube.

Action of Heat.—Substances which contain two or more —COOH, $—SO_3H$, or $—NO_2$ groups generally decompose when

[1] This section is chiefly of interest to those studying for the Pharmaceutical Chemist Qualifying Examination, or for a degree in pharmacy.

they are heated, unless they have a low molecular weight; as also do sugars, glucosides, and metallic salts.

Action of Reagents

Cold Sodium Carbonate Solution.—(*a*) Acids pass into solution with effervescence; when they are insoluble in water, they are reprecipitated on addition of a mineral acid.

(*b*) Ammonium salts give ammonia.

(*c*) Anhydrides *may* pass into soluble salts.

(*d*) Salts of bases (organic or inorganic) are decomposed.

Cold Sodium Hydroxide Solution.—In addition to (*a*), (*b*), (*c*), and (*d*), phenols pass into soluble phenates.

Boiling Sodium Hydroxide Solution.—Hydrolyses esters, amides, and anhydrides. Resinifies aldehydes (and sugars).

Cold Dilute Hydrochloric Acid.—Bases pass into soluble salts, and, if insoluble in water, are reprecipitated on addition of sodium hydroxide.

Ferric Chloride Solution.—Gives colour reactions with phenols and some of their derivatives.

Tests for Elements

Apply the tests for halogens (copper-wire test and sodium fusion), nitrogen, sulphur, and metals.

Substances which contain Nitrogen.—Ammonium salts, amides, amines (test whether primary, secondary, or tertiary), and nitro-compounds (also cyanides, cyanohydrins, oximes, hydrazones, imides, etc.). Nitro-compounds are usually yellow, and decompose with a puff when heated: reduce to a primary base and identify this.

Substances which contain Sulphur.—Alkyl sulphuric acids and their salts. Sulphonic acids and their derivatives. Sodium bisulphite compounds of aldehydes and ketones.

Miscellaneous Tests

Heat with Soda-lime.——COOH groups are displaced by hydrogen, and vapours with characteristic odours may be evolved (for example, benzene from benzoic acid, and phenol from salicylic acid).

Heat with Zinc Dust.—The substance may be decomposed with evolution of vapours with characteristic odours (for example, cyclic bases from alkaloids). Phenols may be reduced, with evolution of hydrocarbon vapours.

Tests for Unsaturated Compounds.—Treat with bromine in absence of water, when additive products are formed (in presence of water, bromine may act as an oxidising agent). Treat with

sodium carbonate solution and a few drops of potassium permanganate (unsaturated compounds reduce alkaline permanganate in the cold).

In the identification of salts, amides, and esters, it is usually necessary to isolate the acid and identify it. For this purpose amides and esters may be hydrolysed by boiling with a dilute solution of sodium hydroxide under a reflux condenser. Substituted amides (*e.g.* acetanilide) are often more easily hydrolysed by means of 50 per cent sulphuric acid.

In the case of solids, the melting-point serves as a final test when the identity of the substance is practically proved.

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APPROXIMATE ATOMIC WEIGHTS

Aluminium	Al	27
Antimony	Sb	120
Arsenic	As	75
Barium	Ba	137
Bismuth	Bi	208
Boron	B	11
Bromine	Br	80
Calcium	Ca	40
Carbon	C	12
Chlorine	Cl	35·5
Chromium	Cr	52
Copper	Cu	63·5
Hydrogen	H	1
Iodine	I	127
Iron	Fe	56
Lead	Pb	207
Lithium	Li	7
Magnesium	Mg	24
Manganese	Mn	55
Mercury	Hg	200·5
Nitrogen	N	14
Oxygen	O	16
Phosphorus	P	31
Potassium	K	39
Silver	Ag	108
Sodium	Na	23
Strontium	Sr	87·5
Sulphur	S	32
Tin	Sn	119
Zinc	Zn	65·5

INDEX

Latin names of official substances in heavy type.
Where two or more references are given, the most important is printed in heavy type.